EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	734	(514/304).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2007/10/19 08:29
L2	135	L1 AND TROPANE	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2007/10/19 08:29
L3	10	l2 and CCR5	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2007/10/19 08:29

Connecting via Winsock to STN

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TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	JUL 02	LMEDLINE coverage updated
NEWS 3	JUL 02	SCISEARCH enhanced with complete author names
NEWS 4	JUL 02	CHEMCATS accession numbers revised
NEWS 5	JUL 02	CA/CAplus enhanced with utility model patents from China
NEWS 6	JUL 16	CAplus enhanced with French and German abstracts
NEWS 7	JUL 18	CA/CAplus patent coverage enhanced
NEWS 8	JUL 26	USPATFULL/USPAT2 enhanced with IPC reclassification
NEWS 9	JUL 30	USGENE now available on STN
NEWS 10	AUG 06	CAS REGISTRY enhanced with new experimental property tags
NEWS 11	AUG 06	BEILSTEIN updated with new compounds
NEWS 12	AUG 06	FSTA enhanced with new thesaurus edition
NEWS 13	AUG 13	CA/CAplus enhanced with additional kind codes for granted patents
NEWS 14	AUG 20	CA/CAplus enhanced with CAS indexing in pre-1907 records
NEWS 15	AUG 27	Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB
NEWS 16	AUG 27	USPATOLD now available on STN
NEWS 17	AUG 28	CAS REGISTRY enhanced with additional experimental spectral property data
NEWS 18	SEP 07	STN AnaVist, Version 2.0, now available with Derwent World Patents Index
NEWS 19	SEP 13	FORIS renamed to SOFIS
NEWS 20	SEP 13	INPADOCDB enhanced with monthly SDI frequency
NEWS 21	SEP 17	CA/CAplus enhanced with printed CA page images from 1967-1998
NEWS 22	SEP 17	CAplus coverage extended to include traditional medicine patents
NEWS 23	SEP 24	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS 24	OCT 02	CA/CAplus enhanced with pre-1907 records from Chemisches Zentralblatt

NEWS EXPRESS 19 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 08:38:21 ON 19 OCT 2007

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 08:38:30 ON 19 OCT 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 18 OCT 2007 HIGHEST RN 950981-10-9
DICTIONARY FILE UPDATES: 18 OCT 2007 HIGHEST RN 950981-10-9

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

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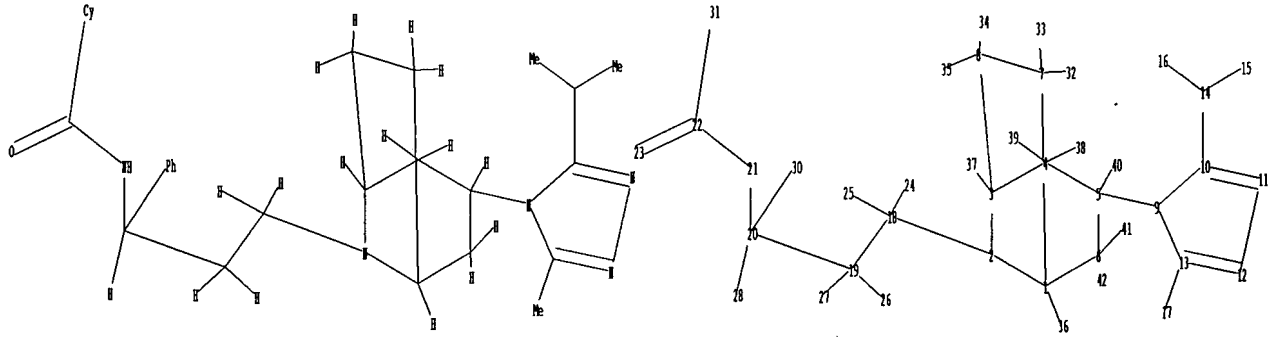

chain nodes :
14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 30 31 32 33 34 35 36 37 38 39 40 41 42
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13
chain bonds :
1-36 2-18 3-37 4-38 4-39 5-9 5-40 6-41 6-42 7-32 7-33 8-34 8-35 10-14 13-17 14-15 14-16 18-19 18-24 18-25 19-20 19-26 19-27 20-21 20-28 20-30 21-22 22-23 22-31

ring bonds :
1-2 1-6 1-7 2-3 3-4 3-8 4-5 5-6 7-8 9-10 9-13 10-11 11-12 12-13
exact/norm bonds :
1-2 1-6 2-3 2-18 3-4 4-5 5-6 5-9 9-10 9-13 10-11 11-12 12-13 20-21
21-22 22-23 22-31
exact bonds :
1-7 1-36 3-8 3-37 4-38 4-39 5-40 6-41 6-42 7-8 7-32 7-33 8-34 8-35
10-14 13-17 14-15 14-16 18-19 18-24 18-25 19-20 19-26 19-27 20-28 20-30
isolated ring systems :
containing 1 : 9 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS
19:CLASS 20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS
27:CLASS 28:CLASS 30:CLASS 31:Atom 32:CLASS 33:CLASS 34:CLASS 35:CLASS
36:CLASS 37:CLASS 38:CLASS 39:CLASS 40:CLASS 41:CLASS 42:CLASS

L1 STRUCTURE UPLOADED

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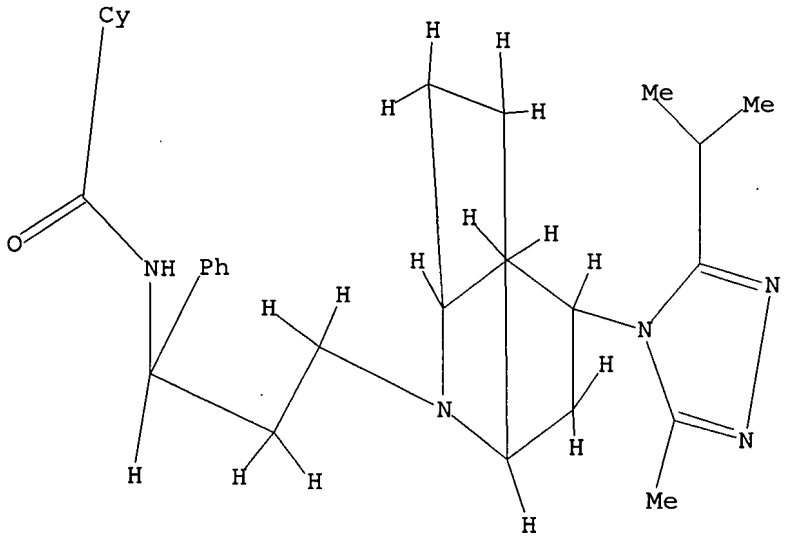
L1 STR



Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SEARCH INITIATED 08:38:47 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 13 TO ITERATE

100.0% PROCESSED 13 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 44 TO 476
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 08:38:51 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 273 TO ITERATE

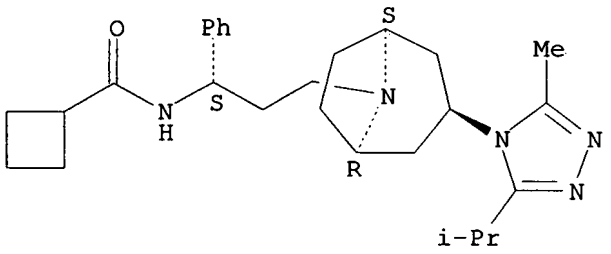
100.0% PROCESSED 273 ITERATIONS 4 ANSWERS
SEARCH TIME: 00.00.01

L3 4 SEA SSS FUL L1

=> d scan

L3 4 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN
IN Cyclobutanecarboxamide, N-[(1S)-3-[(3-endo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]-
MF C27 H39 N5 O

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	172.10	172.31

FILE 'CAPLUS' ENTERED AT 08:39:18 ON 19 OCT 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 19 Oct 2007 VOL 147 ISS 18
FILE LAST UPDATED: 18 Oct 2007 (20071018/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

```
=> s l3 full
L4          78 L3

=> s l4 and CCR5
         5012 CCR5
L5         60 L4 AND CCR5

=> s l5 and HIV
        74692 HIV
          100 HIVS
        74709 HIV
                (HIV OR HIVS)
L6         54 L5 AND HIV

=> d ibib abs hitstr tot

L6   ANSWER 1 OF 54  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2007:941806  CAPLUS
DOCUMENT NUMBER:          147:292172
TITLE:                    Sequential use of viral entry inhibitors to prevention
                          the infection of T lymphocytes by human
                          immunodeficiency virus
INVENTOR(S):              Duensing, Thomas; Fung, Sek Chung Michael; Stanley,
                          Lewis
PATENT ASSIGNEE(S):       Tanox, Inc., USA
SOURCE:                   PCT Int. Appl., 42pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     WO 2007094983         A2    20070823    WO 2007-US2991          20070203
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN,
             KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK,
             MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO,
             RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT,
             TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
PRIORITY APPLN. INFO.:                    US 2006-764840P     P  20060203
                                          US 2006-837975P     P  20060816
AB   The present invention is based upon the surprising discovery that exposure
     of a non-resistant human immunodeficiency virus (HIV) to a first
     entry inhibitor, such as an anti-CD4 antibody or a co- receptor inhibitor,
     which like all current HIV drugs selects for mutations that
     result in a resistant HIV, surprisingly results in HIV
     viruses much more susceptible to neutralization by a second entry
     inhibitor, such as soluble CD4 (sCD4) or an HIV gp41 inhibitor.
     Therefore, the present invention provides methods and compns. for
```

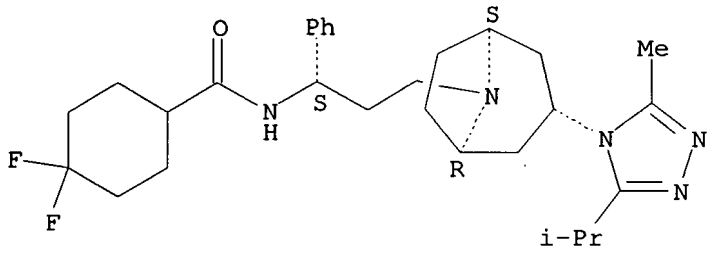
inhibiting HIV-I infection in a subject that overcomes the problem of drug resistance.

IT 376348-65-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as HIV entry inhibitor; sequential use of viral entry inhibitors to prevention infection of T lymphocytes by human immunodeficiency virus)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 2 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2007:851907 CAPLUS

TITLE: Advances in the research of chemokine receptors antagonists as anti-HIV agents

AUTHOR(S): Guo, Xiaojuan; Li, Shaoshun

CORPORATE SOURCE: School of Pharmacy, Shanghai Jiaotong University, Shanghai, 200030, Peop. Rep. China

SOURCE: Zhongguo Yaowu Huaxue Zazhi (2006), 16(2), 122-128
CODEN: ZYHZEF; ISSN: 1005-0108

PUBLISHER: Zhongguo Yaowu Huaxue Zazhi Bianjibu

DOCUMENT TYPE: Journal; General Review

LANGUAGE: Chinese

AB Chemokine receptors such as CCR5 and CXCR4 were found as coreceptor to enter the host cell by HIV. The research of antagonist of chmnokine receptors became a new field of anti-HIV agents. Many potent compds. would lead to the development of novel types of effective antiviral drug. The progress of antagonists of chemokine receptors (CCR5 and CXCR4) as anti-HIV agents was reviewed.

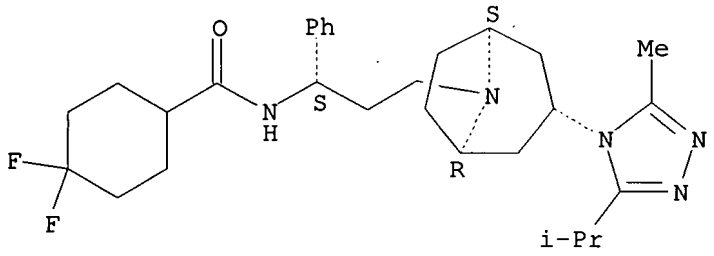
IT INDEXING IN PROGRESS

IT 376348-65-1, UK-427857
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(advances in the research of chemokine receptors antagonists as anti-HIV agents)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



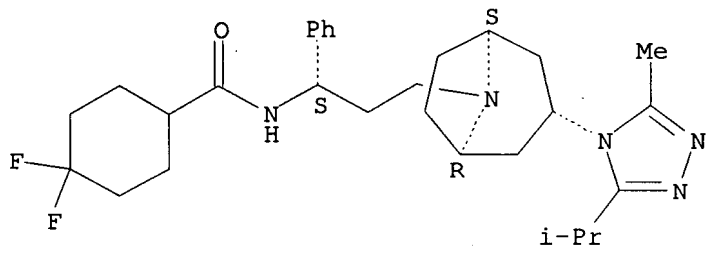
L6 ANSWER 3 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:848300 CAPLUS
DOCUMENT NUMBER: 147:313878
TITLE: CCR5 inhibitors: promising yet challenging
AUTHOR(S): Clotet, Bonaventura
CORPORATE SOURCE: AIDS Care Unit and irsiCaixa Retrovirology Laboratory, Hospital Germans Trias i Pujol, Universitat Autonoma de Barcelona, Badalona, Spain
SOURCE: Journal of Infectious Diseases (2007), 196(2), 178-180
CODEN: JIDIAQ; ISSN: 0022-1899
PUBLISHER: University of Chicago Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. The research of Gulick et al. (2007) entitled "Phase 2 study of the safety and efficacy of vicriviroc, a CCR5 inhibitor, in HIV-1-infected, treatment-experienced patients: AIDS Clin. Trials Group 5211" is reviewed with commentary and refs. Previous studies conducted with maraviroc plus optimized background therapy (OBT) in a treatment-experienced population, harboring only CCR5 tropic virus, have shown significantly superior virol. control and increases in CD4 cell count compared with placebo plus OBT. Gulick et al. also reported a potent virol. suppression through 24 wk, further supporting the anti-HIV-1 activity of the CCR5 inhibitor family. However, a slightly larger number of malignancies in antiretroviral (ARV)-experienced subjects receiving an optimized ARV regimen (OR) plus vicriviroc than in those treated with an OR plus placebo were observed These findings helped to clarify the role of CCR5 entry inhibitors in HIV therapeutics.

IT 376348-65-1, Maraviroc
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chemokine receptor 5 inhibitor maraviroc might be effective in patient infected with human immunodeficiency virus)

RN 376348-65-1 CAPLUS
CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

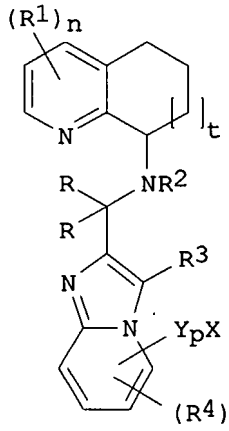
L6 ANSWER 4 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:845963 CAPLUS
DOCUMENT NUMBER: 147:211887
TITLE: Preparation of imidazo[1,2-a]pyridine compds. useful in the treatment of HIV infection and other chemokine receptor-mediated diseases
INVENTOR(S): Gudmundsson, Kristjan; Boggs, Sharon Davis; Miller, John Franklin; Svolto, Angilique Christina
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 148pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007087549	A2	20070802	WO 2007-US60939	20070124

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2006-761892P P 20060125
OTHER SOURCE(S): MARPAT 147:211887
GI



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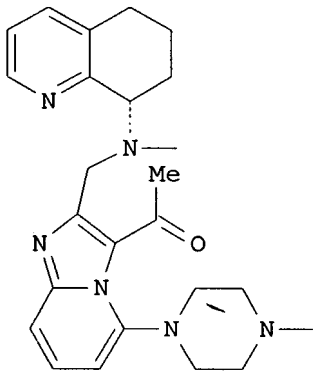


II

AB The present invention provides compds. of general formula I (wherein t = 0-2; each R independently is H, C1-C8 alkyl, C2-C6 alkenyl,etc.; each R1 independently is halo, C1-8 haloalkyl, etc.; n = 0-2; m = 0-2;R2 is H,

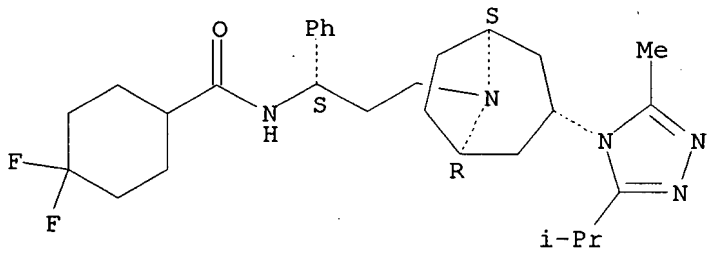
C1-C8 alkyl, C2-C6 alkenyl,etc.; R3 is halogen, substituted amino, etc.; each R4 independently is halogen, C1-C8 haloalkyl, etc.) that demonstrate protective effects on target cells from HIV infection in a manner as to bind to chemokine receptor, and which affect the binding of the natural ligand or chemokine to a receptor such as CXCR4 of a target cell. The compds. of the invention are also useful for treating other diseases, such as rheumatoid arthritis, inflammation, and cancer. Example compound II was prepared by conversion of the ethanol intermediate (preparation given) to the ethanone product. In the HOS HIV-1 infectivity assay, II had an activity level < 100nM.

IT 376348-65-1, UK 427857
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of imidazo[1,2-a]pyridine compds. useful in treatment of HIV infection and other chemokine receptor-mediated diseases)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 5 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2007:845883 CAPLUS
DOCUMENT NUMBER: 147:235169
TITLE: Imidazo[1,2-a]pyridine-3-carboxamides as anti-HIV agents and their preparation, pharmaceutical compositions and their use in monotherapy and in combination therapy of diseases
INVENTOR(S): Gudmundsson, Kristjan; Turner, Elizabeth Madalena
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA; Svolto, Angilique Christina
SOURCE: PCT Int. Appl., 104pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007087548	A2	20070802	WO 2007-US60938	20070124
WO 2007087548	A9	20070927		

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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: US 2006-761883P P 20060125
OTHER SOURCE(S): MARPAT 147:235169

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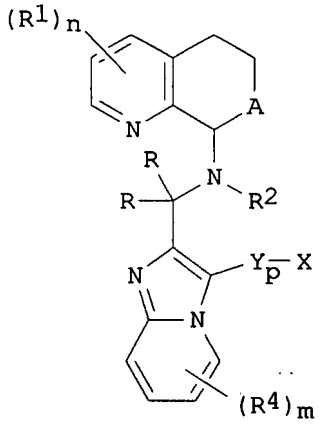

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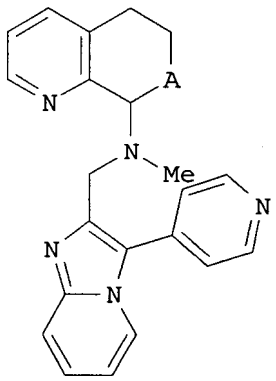


II

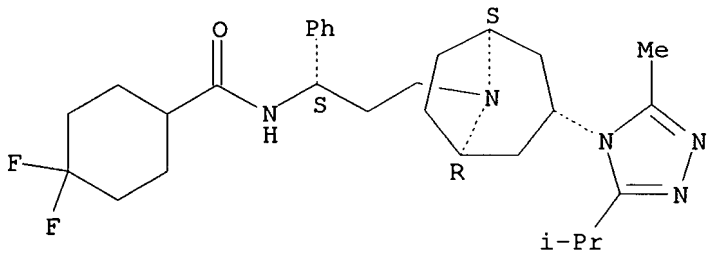
AB The invention provides compds. of formula I including salts, solvates, and pharmaceutically acceptable derivs. thereof, pharmaceutical formulations containing them, processes for their preparation, and methods of treatment using them. Compds. of formula I wherein A is (CH2)0-2; each R is independently H, C1-8 (halo)alkyl, C2-8 alkenyl, C2-6 alkynyl, C3-8 cycloalkyl, etc.; ech R1 is independently halo, C1-8 (halo)alkyl, C2-8 alkenyl, C2-6 alkynyl, C3-8 cycloalkyl, C3-8 cycloalkenyl, etc.; n and m are independently 0, 1 and 2; R2 is H, C1-8 (halo)alkyl, C3-8 cycloalkyl, C2-6 alkenyl, C2-6 alkynyl, etc.; p is 0 and 1; Y is NH and derivs., O, CONH and derivs., NHCO and derivs., CO, CO2, NHCONH and derivs., S, SO, SO2, etc.; X is (un)substituted (hetero)arylamine, (un)substituted (hetero)aryl, (un)substituted heterocyclyl, etc.; R4 is halo, C1-8 (halo)alkyl, C2-6 alkenyl, C2-6 alkynyl, C2-8 cycloalkyl, OH and derivs., CN, NO2, etc.; and their pharmaceutically acceptable derivs. thereof, are claimed. Example compound II was prepared by a multistep procedure (procedure given). All the invention compds. were evaluated for their anti-HIV activity. From the assay, it was determined that the tested compds. exhibited IC50 values of about 1 nM to about 50 μM.

IT 376348-65-1, Maraviroc
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of imidazopyridinecarboxamides as anti-HIV agents useful in monotherapy and in combination therapy of diseases)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 6 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:845813 CAPLUS
DOCUMENT NUMBER: 147:227133
TITLE: Synergistic compositions for treating HIV
INVENTOR(S): Ji, Changhua; Sankuratri, Suryanarayana
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 42pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007085567	A2	20070802	WO 2007-EP50527	20070119

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

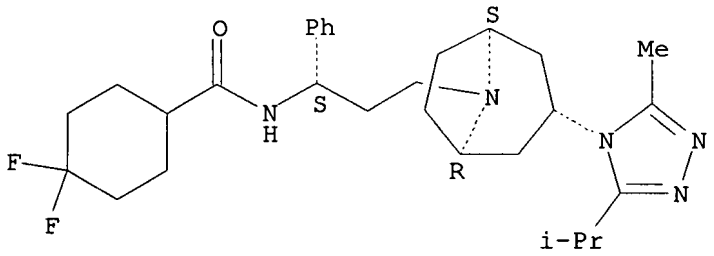
PRIORITY APPLN. INFO.: US 2006-772094P P 20060130
OTHER SOURCE(S): MARPAT 147:227133

AB Synergistic pharmaceutical compns. for treating or preventing HIV -1 infections comprising anti-CCR5 monoclonal antibodies and CCR5 antagonists, viral fusion inhibitors or viral attachment inhibitors are disclosed. The compns. exhibit significant greater activity than is anticipated from the activity of either component alone. Also provided are methods for treating or preventing HIV-1 using the same.

IT 376348-65-1, UK 427857
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synergistic compns. for treating HIV-1 infections using anti-CCR5 monoclonal antibodies and CCR5 antagonists and viral fusion and attachment inhibitors)

RN 376348-65-1 CAPLUS
CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



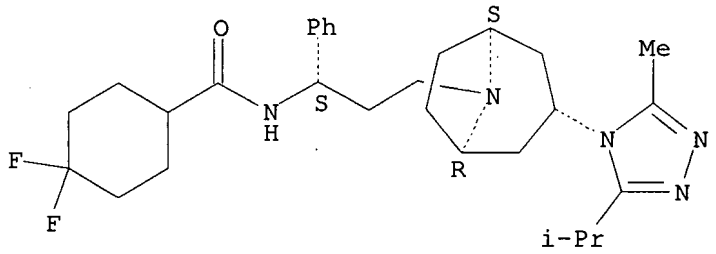
L6 ANSWER 7 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:748017 CAPLUS
DOCUMENT NUMBER: 147:291401
TITLE: CCR5 small-molecule antagonists and monoclonal antibodies exert potent synergistic antiviral effects by cobinding to the receptor
AUTHOR(S): Ji, Changhua; Zhang, Jun; Dioszegi, Marianna; Chiu, Sophie; Rao, Eileen; de Rosier, Andre; Cammack, Nick; Brandt, Michael; Sankuratri, Surya
CORPORATE SOURCE: Department of Viral Diseases, Roche Palo Alto, Palo Alto, CA, USA
SOURCE: Molecular Pharmacology (2007), 72(1), 18-28
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A panel of four CCR5 monoclonal antibodies (mAbs) recognizing different epitopes on CCR5 was examined in CCR5-mediated cell-cell fusion assay, alone or in combination with a variety of small mol. CCR5 antagonists. Although no antagonism was observed between any of the CCR5 inhibitors, surprisingly potent synergy was observed between CCR5 mAbs and antagonists, and the synergistic activity was confirmed in other antiviral assays. Strong synergy was also observed between CCR5 inhibitors and the human immunodeficiency virus (HIV) fusion inhibitor enfuvirtide. There was no synergy observed between small mol. CCR5 inhibitors; however, potent synergy was observed between mAbs recognizing different parts of CCR5. In all synergistic combinations, greater synergy was achieved at higher percent inhibition levels. A neg. correlation was found between the degree of synergy between the two classes of CCR5 inhibitors and the ability to compete each other for binding to the receptor. For example, the greatest synergy, observed between the mAb ROAb13 and the small mol. inhibitor maraviroc, did not interfere with binding to CCR5 for either inhibitor, whereas no synergy was found between mAb 45523 and maraviroc, which do compete for binding to CCR5. In addition, in contrast to a recent report, the CCR5 inhibitors tested here were found to inhibit the same stage of HIV entry. Based on the data presented here, we hypothesize that CCR5 inhibitors exert synergistic antiviral actions through a cobinding mechanism.

IT 376348-65-1, Maraviroc
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CCR5 small-mol. antagonists and monoclonal antibodies exert potent synergistic antiviral effects by cobinding to the receptor)

RN 376348-65-1 CAPLUS
CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

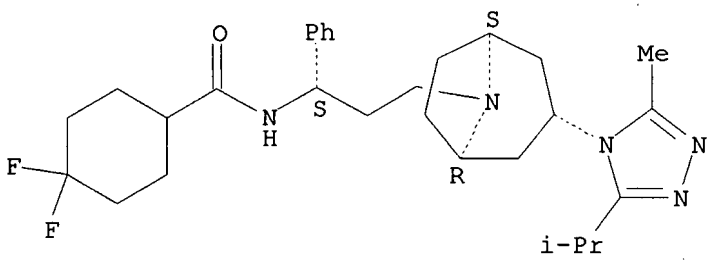
L6 ANSWER 8 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:657188 CAPLUS
TITLE: Antiretroviral treatment of HIV infection: Swedish recommendations 2007
AUTHOR(S): Josephson, Filip; Albert, Jan; Flamholc, Leo; Gisslen, Magnus; Karlstroem, Olof; Lindgren, Susanne-Rosa; Naver, Lars; Sandstroem, Eric; Svedhem-Johansson, Veronica; Svennerholm, Bo; Soennerborg, Anders
CORPORATE SOURCE: Department of Clinical Pharmacology, Karolinska University Hospital, Uppsala, Swed.
SOURCE: Scandinavian Journal of Infectious Diseases (2007), 39(6-7), 486-507
CODEN: SJIDB7; ISSN: 0036-5548
PUBLISHER: Informa Healthcare
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. On 3 previous occasions, in 2002, 2003 and 2005, the Swedish Medical Products Agency (Laekemedelsverket) and the Swedish Reference Group for Antiviral Therapy (RAV) have jointly published recommendations for the treatment of HIV infection. An expert group, under the guidance of RAV, has now revised the text again. Since the publication of the previous treatment recommendations, 1 new drug for the treatment of HIV has been approved - the protease inhibitor (PI) darunavir (Prezista). Furthermore, 3 new drugs have become available: the integrase inhibitor raltegravir (MK-0518), the CCR5-inhibitor maraviroc (Celsentri), both of which have novel mechanisms of action, and the non-nucleoside reverse transcriptase inhibitor (NNRTI) etravirine (TMC-125). The new guidelines differ from the previous ones in several respects. The most important of these are that abacavir is now preferred to tenofovir and zidovudine, as a first line drug in treatment-naive patients, and that initiation of antiretroviral treatment is now recommended before the CD4 cell count falls below 250/μl, rather than 200/μl. Furthermore, recommendations on the treatment of HIV infection in children have been added to the document. As in the case of the previous publication, recommendations are evidence-graded in accordance with the Oxford Center for Evidence Based Medicine, 2001.

IT 376348-65-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CCR5-inhibitor Celsentri showed therapeutic potential against patient infected with human immunodeficiency virus)

RN 376348-65-1 CAPLUS
CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 108 THERE ARE 108 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

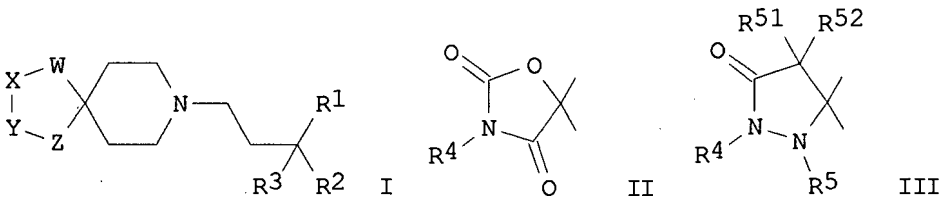
L6 ANSWER 9 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:642553 CAPLUS
DOCUMENT NUMBER: 147:72745
TITLE: Preparation of novel spiropiperidine compounds for the modulation of chemokine receptor activity
INVENTOR(S): Moinet, Christophe; Courchesne, Marc
PATENT ASSIGNEE(S): Virochem Pharma Inc., Can.
SOURCE: PCT Int. Appl., 81pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007065256	A1	20070614	WO 2006-CA1981	20061205

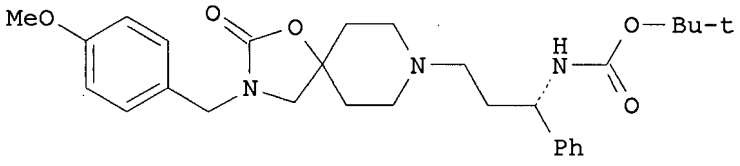
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-742545P P 20051206
OTHER SOURCE(S): MARPAT 147:72745
GI



I II III



IV

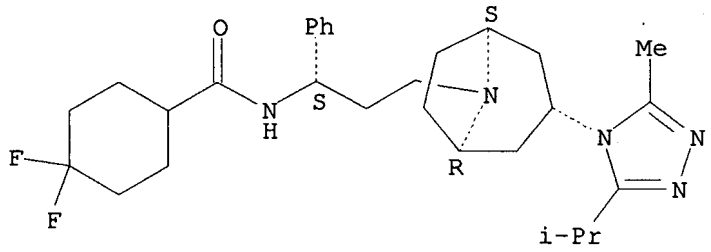
AB The title compds. I [ring containing W, X, Y and Z = II, III, etc.; R1 = NR6C(O)R7, NR6C(O)OR7, etc.; R2 = alkyl, alkenyl, aryl, etc.; R3 = H, alkyl, aryl; R4, R5, R51, R52 = H, alkyl, aryl, etc.; R6 = H, alkyl, alkenyl, alkynyl; R7 = H, alkyl, alkenyl, aryl, etc.], useful for the modulation of CCR5 chemokine receptor activity, particularly in the prevention or treatment of inflammatory diseases, immunoregulatory diseases, organ transplantation reactions and infectious diseases such as HIV infections, were prepared and claimed. E.g., a multi-step synthesis of (S)-IV, starting from tert-Bu 2-oxo-1-oxa-3,8-diaza-spiro[4.5]decane-8-carboxylate and 4-methoxybenzyl chloride, was given. Compds. I have been found to have activity in binding to the CCR5 receptor, generally with an IC50 value of less than 25 μM. Certain compds. I have also been tested in an assay for HIV activity and generally having an IC50 value of less than 1 μM.

IT 376348-65-1, UK-427857
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of novel spiropiperidine compds. as chemokine receptor modulators useful in treatment and prevention of diseases)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 10 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:630737 CAPLUS
DOCUMENT NUMBER: 147:210058

TITLE: Cell surface expression of CCR5 and other host factors influence the inhibition of HIV -1 infection of human lymphocytes by CCR5 ligands

AUTHOR(S): Ketas, Thomas J.; Kuhmann, Shawn E.; Palmer, Ashley; Zurita, Juan; He, Weijing; Ahuja, Sunil K.; Klasse, Per Johan; Moore, John P.

CORPORATE SOURCE: Department of Microbiology and Immunology, Weill Medical College of Cornell University, New York, NY, 10021, USA

SOURCE: Virology (2007), 364(2), 281-290
CODEN: VIRLAX; ISSN: 0042-6822

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

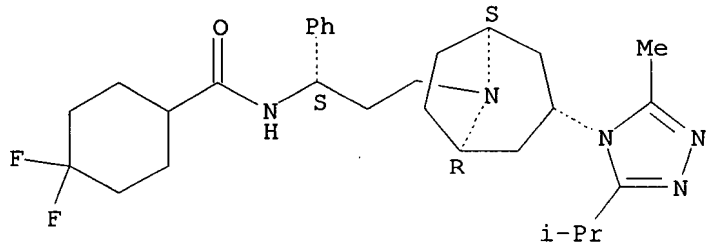
AB Several CCR5 ligands, including small mols. and monoclonal antibodies (MAbs), are being developed as therapies for infection with strains of human immunodeficiency virus type 1 (HIV-1) that use CCR5 for entry (R5 viruses). The efficacy of such therapies could be influenced by inter-individual differences in host factors, such as CCR5 expression levels. To study this, the authors used peripheral blood mononuclear cells (PBMCs) from humans and rhesus macaques. The half-maximal inhibitory concns. (IC50) of the small-mol. CCR5 ligands CMPD167, UK427,857 and SCH-D, and of the PRO 140 MAb, differ by >2 logs in a donor-dependent manner. The authors studied this variation by using flow cytometry to measure CCR5 expression on PBMCs from 6 of the human donors: the IC50 values of both SCH-D and PRO 140 correlated with CCR5 expression. The authors also determined the efficacy of the CCR5 ligands against HIV-1 infection of HeLa-derived cell lines that express CD4 at the same level but vary 2-fold in CCR5 expression (JC.48 and JC.53 cells). The moderately greater CCR5 expression on the JC.53 than the JC.48 cells was associated with proportionately higher median IC50 values for all 4 CCR5 ligands but not for a soluble CD4-based inhibitor or a non-nucleoside reverse transcriptase inhibitor. Thus, differences in CCR5 expression on human PBMCs, which can be affected by CCL3L1 gene dose, may influence the antiviral potency of CCR5 ligands in vitro, but other host factors are also likely to be involved. These host factors may affect the clin. activity of CCR5 inhibitors, including their use as topical microbicides to prevent HIV-1 transmission.

IT 376348-65-1, UK 427857
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CCR5 co-receptor d. influences inhibition of HIV-1 infection of human lymphocytes by CCR5 ligands)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

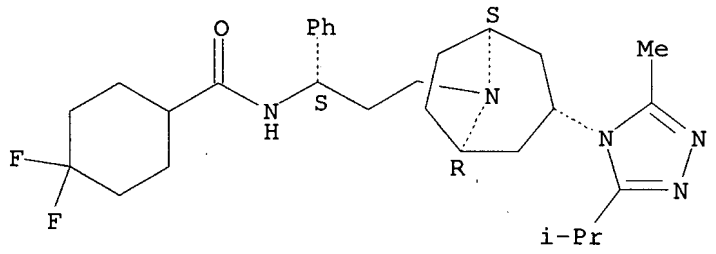
Absolute stereochemistry.



REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:525368 CAPLUS
DOCUMENT NUMBER: 147:124692
TITLE: New HIV drugs edge towards approval
AUTHOR(S): Hadlington, Simon
CORPORATE SOURCE: UK
SOURCE: Chemistry World (2007), 4(4), 14
CODEN: CWHOBI; ISSN: 1473-7604
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Two promising new drugs for treating HIV, the virus that causes AIDS, could receive regulatory approval in the US later this year. The development of the new drugs is significant because each works in a different way from the existing arsenal of anti-HIV products. This could help to overcome the problem of patients developing resistance. The drugs are maraviroc, developed by Pfizer, and raltegravir, from Merck and Co.
IT 376348-65-1, Maraviroc
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(new HIV drugs edge towards approval)
RN 376348-65-1 CAPLUS
CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 12 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:493220 CAPLUS
DOCUMENT NUMBER: 147:132457
TITLE: Assessing theoretical risk and benefit suggested by genetic association studies of CCR5: experience in a drug development programme for maraviroc
AUTHOR(S): Wheeler, Jeremy; McHale, Mary; Jackson, Vicky; Penny, Michelle
CORPORATE SOURCE: Pfizer Research and Development, Sandwich, Kent, UK
SOURCE: Antiviral Therapy (2007), 12(2), 233-245
CODEN: ANTHFA; ISSN: 1359-6535
PUBLISHER: International Medical Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The proliferation of published gene association studies of the CCR5.DELTA.32 mutation is of relevance to drug development of a CCR5 antagonist for HIV, in highlighting potential

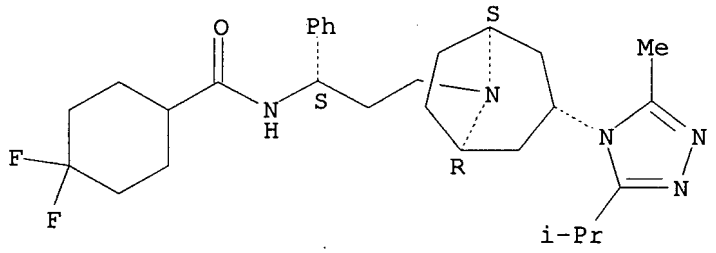
safety concerns. We conducted an initial review of all non-HIV gene association studies of CCR5-Δ32, followed by detailed meta-analyses in the three disease areas most commonly reported. Our review indicated no consistent evidence of increased risk of susceptibility to hepatitis C virus infection or multiple sclerosis among individuals with CCR5-Δ32 mutation, and suggested treatment with a CCR5 inhibitor is unlikely to have related adverse effects. There was, however, evidence to suggest rheumatoid arthritis as a potential therapeutic target for a CCR5 antagonist. Clin. evidence would be required to confirm these findings.

IT 376348-65-1, Maraviroc
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CCR5 antagonist targeted rheumatoid arthritis but not hepatitis C virus infection and multiple sclerosis during maraviroc development program against human immunodeficiency virus infected patient)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:343360 CAPLUS
DOCUMENT NUMBER: 146:519894
TITLE: Novel CCR5 monoclonal antibodies with potent and broad-spectrum anti-HIV activities
AUTHOR(S): Ji, Changhua; Brandt, Michael; Dioszegi, Marianna; Jekle, Andreas; Schwoerer, Stephan; Challand, Steven; Zhang, Jun; Chen, Yun; Zautke, Lisa; Achhammer, Gunthar; Baehner, Monika; Kroetz, Sandra; Heilek-Snyder, Gabrielle; Schumacher, Ralf; Cammack, Nick; Sankuratri, Surya
CORPORATE SOURCE: Department of Viral Diseases, Roche Palo Alto, Palo Alto, CA, 94304, USA
SOURCE: Antiviral Research (2007), 74(2), 125-137
CODEN: ARSRDR; ISSN: 0166-3542
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To identify monoclonal antibodies (mAbs) with high potency and novel recognition sites, more than 25,000 of mouse hybridomas were screened and 4 novel anti-human CCR5 mAbs ROAb12, ROAb13, ROAb14, and ROAb18 showing potent activity in cell-cell fusion (CCF) assay were identified. These mAbs demonstrated potent antiviral activities in both single-cycle HIV infection (IC50 range: 0.16-4.3 μg/mL) and PBMC viral replication (IC50 range: 0.02-0.04 μg/mL) assays. These potent

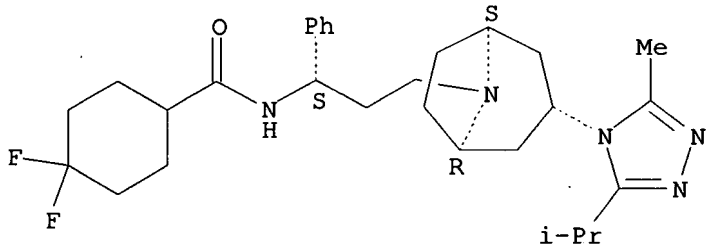
antiviral effects were donor-independent. All 4 mAbs were also highly potent in the PhenoSense assay against 29 HIV isolates covering clade A through G. In all antiviral assays, these mAbs showed potency superior to the previously reported mAb 2D7 in side-by-side comparison studies. All 4 mAbs were also fully active against viruses resistant to HIV fusion inhibitor enfuvirtide and CCR5 antagonist maraviroc. Although ROAb12, ROAb14, and ROAb18 inhibited RANTES, MIP1α and MIP1β binding and cell activation, the other novel mAb ROAb13 was inactive in inhibiting cell activation by these three ligands. Furthermore, highly synergistic antiviral effects were found between mAb ROAb13 and 2D7 or ROAb12. In addition, none of these mAbs showed agonist activity or caused internalization of the CCR5 receptor.

IT 376348-65-1, Maraviroc.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HIV resistant to; novel CCR5 monoclonal antibodies with potent and broad-spectrum anti-HIV activities)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 14 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:329882 CAPLUS
DOCUMENT NUMBER: 146:351292
TITLE: Use of indirubin and its derivatives in the treatment of HIV infection and heart failure
INVENTOR(S): Redfield, Robert; Heredia, Alonso; Davis, Charles E.
PATENT ASSIGNEE(S): University of Maryland Biotechnology Institute Off. of Research Admin/Tech. Dev., USA
SOURCE: PCT Int. Appl., 36pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007033208	A2	20070322	WO 2006-US35559	20060912

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,

IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-716097P P 20050912

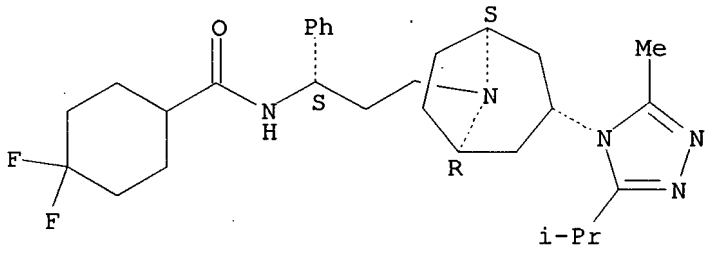
AB Indirubin and its derivs. are described for reduction of replication of human immunodeficiency virus. Indirubin and its derivs. are also described for reducing the effects of heart failure, by administration of indirubin or a functionally active derivative thereof to modify cardiac muscle cell hypertrophy. Indirubin and its functional derivs. may also be employed in antiviral combination therapy compns. containing therapeutically effective chimeric polypeptides containing a virus coat polypeptide sequence and a viral receptor polypeptide sequence wherein the virus coat polypeptide sequence and the viral receptor polypeptide sequence are linked and exhibit ligand/receptor binding affinity.

IT 376348-65-1, UK-427857 376348-65-1D, UK-427857, analogs
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(indirubin and derivs. for treatment of HIV infection and heart failure, and use with other agents)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

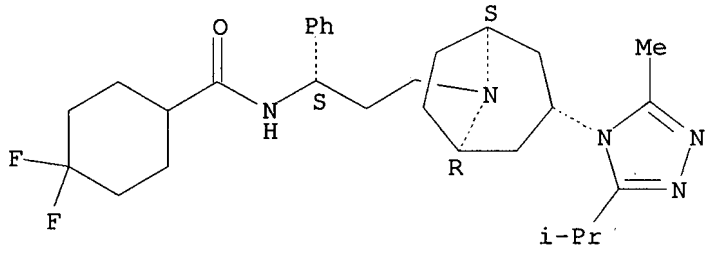
Absolute stereochemistry.



RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 15 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2007:259531 CAPLUS

DOCUMENT NUMBER: 146:316914

TITLE: Imidazo[1,2-a]pyridine compounds as chemokine receptor ligands and their preparation, pharmaceutical compositions and use in the treatment of HIV

infection

INVENTOR(S): Gudmundsson, Kristjan; Boggs, Sharon Davis

PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA

SOURCE: PCT Int. Appl., 91pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007027999.	A2	20070308	WO 2006-US34195	20060830

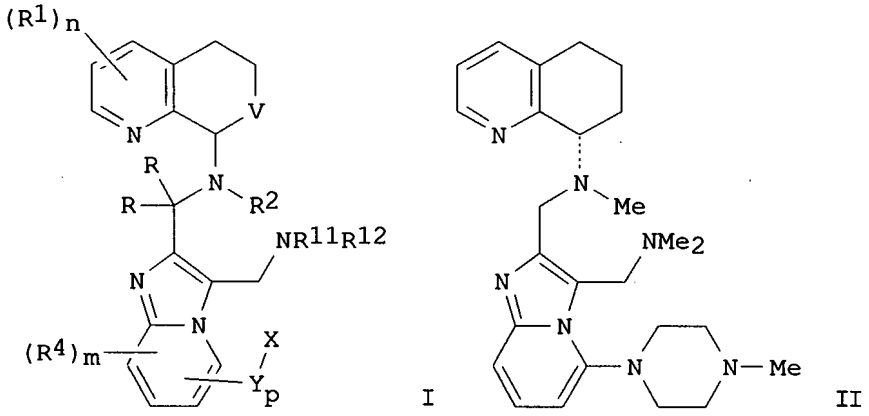
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-713134P P 20050831

OTHER SOURCE(S): MARPAT 146:316914

GI



AB The invention provides compds. of formula I that demonstrate protective effects on target cells from HIV infection in a manner as to bind to chemokine receptor, and which affect the binding of the natural ligand or chemokine to a receptor such as CXCR4 of a target cell. Compds. of formula I wherein V is absent, CH2 and CH2CH2; each R is independently H, C1-8 (halo)alkyl, C2-8 alkenyl, C2-6 alkynyl, C3-8 cycloalkyl, etc.; each R1 and each R4 are independently halo, C1-8 (halo)alkyl, C2-6 alkenyl, C2-6 alkynyl, C3-8 cycloalkyl, etc.; m and n is is 0, 1 and 2; R2 is H, C1-8 (halo)alkyl, C3-8 cycloalkyl, C2-6 alkenyl, C2-6 alkynyl, etc.; Y is NH and derivs., O, CONH and derivs., NHCO and derivs., CO, CO2, NHCONH and derivs., etc.; p is 0 and 1; X is NH2 and derivs.., C1-8 alkylenamino, C3-8 cycloalkylenamino, etc.; R11 and R12 are independently H, C1-8 (halo)alkyl, C2-8 alkenyl, C2-6 alkynyl, C3-8 cycloalkyl, C3-8 cycloalkenyl, etc.; and their pharmaceutically acceptable derivs. thereof,

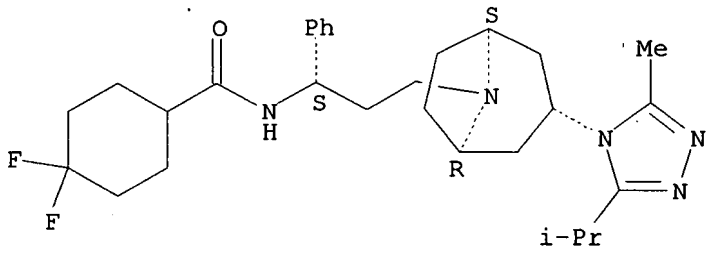
are claimed. Example compound II was prepared by Mannich reaction of (8S)-N-methyl-N-[[5-(4-methyl-1-piperazinyl)imidazo[1,2-a]pyridin-2-yl]methyl]-5,6,7,8-tetrahydro-8-quinolinamine with formaldehyde and dimethylamine. All the invention compds. were evaluated for their HIV infective activity. From the assay, it was determined that compound II exhibited less than 100 nM activity.

IT 376348-65-1, UK 427857
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of imidazopyridine compds. useful in the treatment of HIV infection and other chemokine receptor-mediated diseases)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 16 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2007:207313 CAPLUS

DOCUMENT NUMBER: 146:329986

TITLE: Reduced maximal inhibition in phenotypic susceptibility assays indicates that viral strains resistant to the CCR5 antagonist maraviroc utilize inhibitor-bound receptor for entry

AUTHOR(S): Westby, Mike; Smith-Burchnell, Caroline; Mori, Julie; Lewis, Marilyn; Mosley, Michael; Stockdale, Mark; Dorr, Patrick; Ciaramella, Giuseppe; Perros, Manos

CORPORATE SOURCE: Pfizer Global Research and Development, Sandwich, UK

SOURCE: Journal of Virology (2007), 81(5), 2359-2371
CODEN: JOVIAM; ISSN: 0022-538X

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Maraviroc is a CCR5 antagonist in clin. development as one of a new class of antiretrovirals targeting human immunodeficiency virus type 1 (HIV-1) coreceptor binding. We investigated the mechanism of HIV resistance to maraviroc by using in vitro sequential passage and site-directed mutagenesis. Serial passage through increasing maraviroc concns. failed to select maraviroc-resistant variants from some laboratory-adapted and clin. isolates of HIV-1. However, high-level resistance to maraviroc was selected from three of six primary isolates passaged in peripheral blood lymphocytes (PBL). The SF162 strain acquired resistance to maraviroc in both treated and control cultures; all resistant variants were able to use CXCR4 as a coreceptor. In contrast, maraviroc-resistant virus derived from isolates CC1/85 and RU570 remained CCR5 tropic, as evidenced by susceptibility to the CCR5 antagonist SCH-C, resistance to the CXCR4 antagonist AMD3100, and an inability to replicate in CCR5 Δ32/Δ32 PBL.
Strain-specific mutations were identified in the V3 loop of maraviroc-resistant CC1/85 and RU570. The envelope-encoding region of

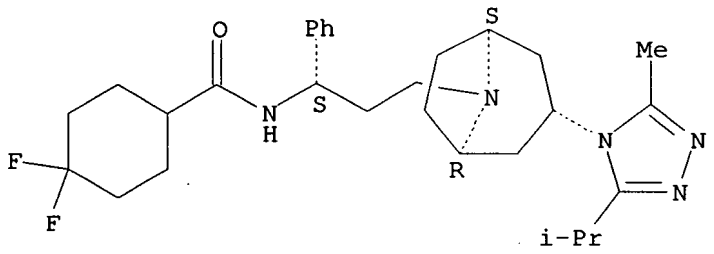
maraviroc-resistant CC1/85 was inserted into an NL4-3 background. This recombinant virus was completely resistant to maraviroc but retained susceptibility to aplaviroc. Reverse mutation of gp120 residues 316 and 323 in the V3 loop (numbering from HXB2) to their original sequence restored wild-type susceptibility to maraviroc, while reversion of either mutation resulted in a partially sensitive virus with reduced maximal inhibition (plateau). The plateaus are consistent with the virus having acquired the ability to utilize maraviroc-bound receptor for entry. This hypothesis was further corroborated by the observation that a high concentration
of maraviroc blocks the activity of aplaviroc against maraviroc-resistant virus.

IT 376348-65-1, Maraviroc
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(reduced maximal inhibition in phenotypic susceptibility assays indicates that viral strains resistant to CCR5 antagonist maraviroc utilize inhibitor-bound receptor for entry)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 17 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:119657 CAPLUS
DOCUMENT NUMBER: 146:182972
TITLE: Methods for reducing viral load in HIV -1-infected patients
INVENTOR(S): Olson, William C.; Maddon, Paul J.; Pevear, Daniel C.; Israel, Robert J.; Murga, Jose D.
PATENT ASSIGNEE(S): Progenics Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 97pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007014114	A2	20070201	WO 2006-US28565	20060721

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG,

US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

US 2007026441	A1	20070201	US 2006-491330	20060721
PRIORITY APPLN. INFO.:			US 2005-702064P	P 20050722
			US 2005-701889P	P 20050723
			US 2005-711528P	P 20050826
			US 2005-715619P	P 20050909

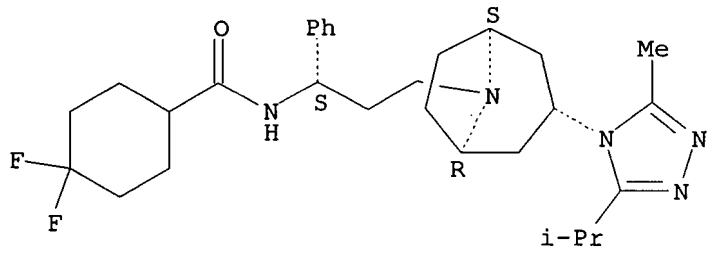
AB The authors disclose a method for reducing viral load in an HIV -1-infected human subject. The method comprises the administration at a predefined intervals of (a) a humanized antibody designated PRO 140, or of (b) an anti-CCR5 receptor monoclonal antibody. The authors also disclose a treatment comprising the administration of (a) a monoclonal antibody which (i) binds to a CCR5 receptor on the surface of the subject's CD4+ cells and (ii) inhibits fusion of HIV-1 to CCR5+CD4+ cells, and (b) a non-antibody CCR5 receptor antagonist, in therapeutic amts.

IT 376348-65-1, UK 427857
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (with anti-CCR5 antibody for combination therapy in human immunodeficiency virus infection)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 18 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2007:61836 CAPLUS
DOCUMENT NUMBER:	146:163092
TITLE:	Pyranopyridines and oxepinopyridines as protectants from HIV infection, their preparation, pharmaceutical compositions, and use in therapy
INVENTOR(S):	Gudmundsson, Kristjan
PATENT ASSIGNEE(S):	Smithkline Beecham Corporation, USA
SOURCE:	PCT Int. Appl., 70pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007008539	A2	20070118	WO 2006-US26239	20060705
WO 2007008539	A3	20070510		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: US 2005-698110P P 20050711
OTHER SOURCE(S): MARPAT 146:163092
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

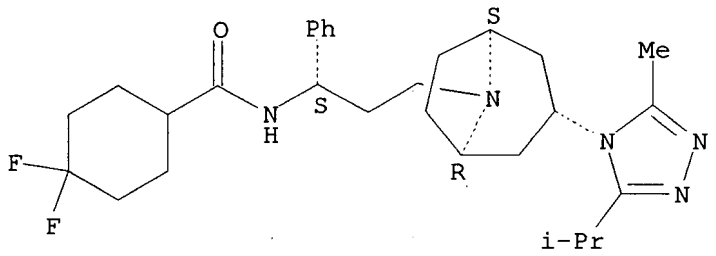
AB The invention relates to compds. of general formula I, which affect the binding of the natural ligand or chemokine to the CXCR4 receptor, thereby exerting protective effects on target cells from HIV infection. In compds. I, X is (un)substituted amino, (un)substituted aminoalkylene, (un)substituted aminoarylene, (un)substituted heterocyclyl, (un)substituted heteroaryl, (un)substituted aminoheterocyclyl, (un)substituted aminoheteroaryl, etc.; Y is a bond, (un)substituted N, O, S, (un)substituted carbamoyl, (un)substituted carbonylamino, carbonyl, carbonyloxy, (un)substituted ureido, S(O)q, (un)substituted S(O)qNH, or (un)substituted NHS(O)q, where q is 0, 1, or 2; Z is CH2 or CH2CH2; each R1 and R4 is independently selected from halo, cyano, nitro, azido, haloalkyl, alkyl, cycloalkyl, (un)substituted aryl, (un)substituted arylamino, (un)substituted heterocyclyl, (un)substituted heteroaryl, (un)substituted aryloxy, etc.; each of n and m is independently 0, 1, or 2; R2 and R3 are independently selected from H, alkyl, haloalkyl, cycloalkyl, (un)substituted aryl, (un)substituted arylalkylene, alkoxyalkylene, alkylsulfonylalkylene, etc.; and each R5 is independently selected from H, alkyl, alkenyl, alkynyl, cycloalkyl, and (un)substituted aryl; including pharmaceutically acceptable derivs. thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a compound I and a pharmaceutically acceptable carrier optionally with at least one addnl. therapeutic agent, as well as to the use of the compns. in the treatment or prophylaxis of a viral infection, such as HIV infection. Reductive amination of pyranopyridinone II with glycine benzyl ester hydrochloride followed by N-methylation and hydrogenation gave glycine derivative III. 3-Chloro-2-nitroaniline was substituted with N,N,N'-trimethylethylenediamine and hydrogenated, resulting in the formation of benzenetriamine IV, which underwent condensation with III to give pyranopyridine V. The compds. of the invention, e.g., V, express anti-HIV activity with IC50 values between 1 nM and 1000 nM (no specific data).

IT 376348-65-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of pyranopyridines and oxepinopyridines as protectants from HIV infection)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 19 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:22573 CAPLUS
DOCUMENT NUMBER: 146:265847
TITLE: Carbohydrate-binding agents efficiently prevent dendritic cell-specific intercellular adhesion molecule-3-grabbing nonintegrin (DC-SIGN)-directed HIV-1 transmission to T lymphocytes
AUTHOR(S): Balzarini, Jan; Van Herrewege, Yven; Vermeire, Kurt; Vanham, Guido; Schols, Dominique
CORPORATE SOURCE: Rega Institute for Medical Research, Katholieke Universiteit Leuven, Louvain, Belg.
SOURCE: Molecular Pharmacology (2007), 71(1), 3-11
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Exposure of HIV-1 to dendritic cell-specific intercellular adhesion mol.-3-grabbing nonintegrin (DC-SIGN)-expressing B-lymphoblast Raji cells (Raji/DC-SIGN) but not to wild-type Raji/0 cells results in the capture of HIV-1 particles to the cells as measured by the quantification of cell-associated p24 antigen. Cocultivation of HIV -1-captured Raji/DC-SIGN cells with uninfected CD4+ T lymphocyte C8166 cells results in abundant formation of syncytia within 36 h after cocultivation. Short preexposure of HIV-1 to carbohydrate-binding agents (CBA) dose dependently prevents the Raji/DC-SIGN cells from efficiently binding the virus particles, and no syncytia formation occurs upon subsequent cocultivation with C8166 cells. Thus, the mannose-specific, the plant lectins Hippeastrum hybrid agglutinin (HHA), Galanthus nivalis agglutinin (GNA), Narcissus pseudonarcissus agglutinin; and Cymbidium agglutinin (CA); the procaryotic cyanovirin-N (CV-N); and the monoclonal antibody (2G12) and N-acetylglucosamine-specific (i.e., the plant lectin Urtica dioica agglutinin) CBAs efficiently abrogate the DC-SIGN-directed HIV-1 capture and subsequent transmission to T lymphocytes. In this assay, the CD4-down-regulating cyclotriazodisulfonamide derivative, the CXCR4 and CCR5 coreceptor antagonists 1-[[4-(1,4,8,11-tetrazacyclotetradec-1-ylmethyl)phenyl]methyl]-1,4,8,11-tetrazacyclotetradecane (AMD3100) and maraviroc, the gp41-binding enfuvirtide, and the polyanionic substances dextran sulfate (Mr 5000), sulfated polyvinyl alc., and the naphthalene sulfonate polymer PRO-2000 were markedly less efficient or even completely ineffective. Similar observations were made in primary monocyte-derived dendritic cell cultures that were infected with HIV-1 particles that had been shortly pre-exposed to the CBAs CV-N, CA, HHA, and GNA and the polyanions DS-5000 and PRO-2000. The potential of CBAs, but not polyanions and other structural/functional classes of entry inhibitors, to impair DC-SIGN-expressing cells in their capacity of transmitting HIV to T lymphocytes might be an important property to be taken into consideration in the eventual choice to move microbicide candidate drugs to the clin. setting.

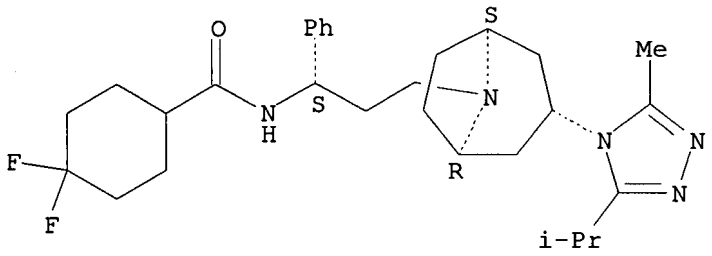
IT 376348-65-1, Maraviroc

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(carbohydrate-binding agents efficiently prevent dendritic cell-specific intercellular adhesion mol.-3-grabbing nonintegrin (DC-SIGN)-directed HIV-1 transmission to T lymphocytes)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 20 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:1086354 CAPLUS

DOCUMENT NUMBER: 145:369300

TITLE: Potent antiviral synergy between monoclonal antibody and small-molecule CCR5 inhibitors of human immunodeficiency virus type 1

AUTHOR(S): Murga, Jose D.; Franti, Michael; Pevear, Daniel C.; Maddon, Paul J.; Olson, William C.

CORPORATE SOURCE: Progenics Pharmaceuticals, Inc., Tarrytown, NY, 10591, USA

SOURCE: Antimicrobial Agents and Chemotherapy (2006), 50(10), 3289-3296
CODEN: AMACCQ; ISSN: 0066-4804

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The chemokine receptor CCR5 provides a portal of entry for human immunodeficiency virus type 1 (HIV-1) into susceptible CD4+ cells. Both monoclonal antibody (MAb) and small-mol. CCR5 inhibitors have entered human clin. testing, but little is known regarding their potential interactions. We evaluated the interactions between CCR5 MAbs, small-mol. CCR5 antagonists, and inhibitors of HIV-1 gp120, gp41, and reverse transcriptase in vitro. Inhibition data were analyzed for cooperative effects using the combination index (CI) method and stringent statistical criteria. Potent, statistically significant antiviral synergy was observed between the CCR5 MAb PRO 140 and the small-mol. CCR5 antagonists maraviroc (UK-427,857), vicriviroc (SCH-D), and TAK-779. High-level synergy was observed consistently across various assay systems, HIV -1 envelopes, CCR5 target cells, and inhibition levels. CI values ranged from 0.18 to 0.64 and translated into in vitro dose redns. of up to 14-fold. Competition binding studies revealed nonreciprocal patterns of CCR5 binding by MAb and small-mol. CCR5 inhibitors, suggesting that synergy occurs at the level of receptor binding. In addition, both PRO 140 and maraviroc synergized with the chemokine RANTES, a natural ligand for CCR5; however, additive effects were observed for both small-mol. CCR5 antagonists and PRO

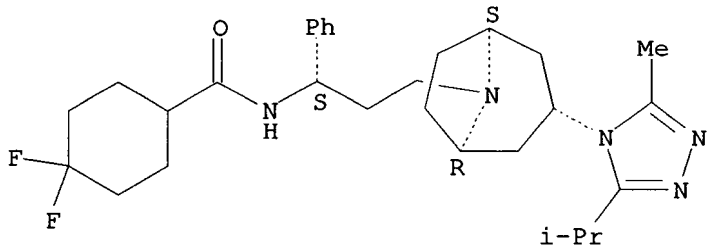
140 in combination with other classes of HIV-1 inhibitors. The findings provide a rationale for clin. exploration of MAb and small-mol. CCR5 inhibitors in novel dual-CCR5 regimens for HIV-1 therapy.

IT 376348-65-1, Maraviroc
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(potent antiviral synergy between monoclonal antibody and small-mol. CCR5 inhibitors of human immunodeficiency virus type 1)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 21 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:984727 CAPLUS
DOCUMENT NUMBER: 146:513210
TITLE: Future of maraviroc and other CCR5 antagonists
AUTHOR(S): Overton, E. Turner; Powderly, William G.
CORPORATE SOURCE: Washington University School of Medicine, St Louis, MO, USA
SOURCE: Future Virology (2006), 1(5), 605-613
CODEN: FVUIAM; ISSN: 1746-0794
PUBLISHER: Future Medicine Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

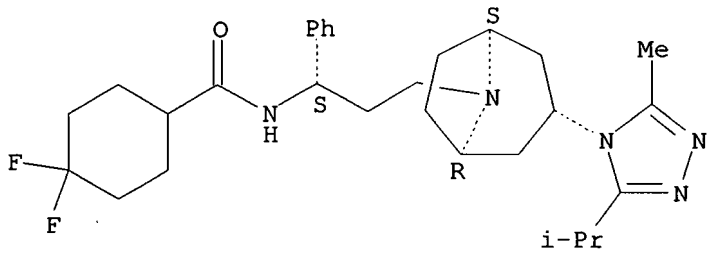
AB A review. Current antitretroviral therapy, although very effective in reducing the mortality and morbidity of HIV infection, remains challenged by the emergence of antiviral resistance. The development of a new class of antiretroviral drugs, based on the unique use of the chemokine receptor, CCR5, for initial viral entry into cells, offers an opportunity to overcome current resistance. Chemokine receptor antagonists, of which maraviroc is the leading product in development, are active in vitro and in vivo against both wild-type HIV and strains resistant to current drugs. Current Phase III trials help determine their place in HIV therapeutics, as well as the relative importance of viruses that utilize an alternative receptor, CXCR4.

IT 376348-65-1, Maraviroc
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chemokine receptor 5 antagonist maraviroc was active in human immunodeficiency virus-infected patient)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

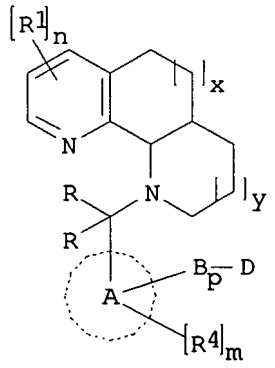
L6 ANSWER 22 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:945669 CAPLUS
DOCUMENT NUMBER: 145:336055
TITLE: Preparation of heteroarylmethyl substituted octahydro-1,10-phenanthrolines and analogs for treating diseases modulated by a chemokine receptor (CXCR4)
INVENTOR(S): Gudmundsson, Kristjan; Catalano, John, G.; Svolto, Angilique
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 183pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006096444	A2	20060914	WO 2006-US7395	20060301
WO 2006096444	A3	20070927		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: US 2005-658530P P 20050304
OTHER SOURCE(S): MARPAT 145:336055
GI



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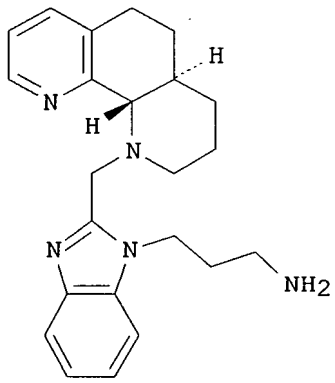


II

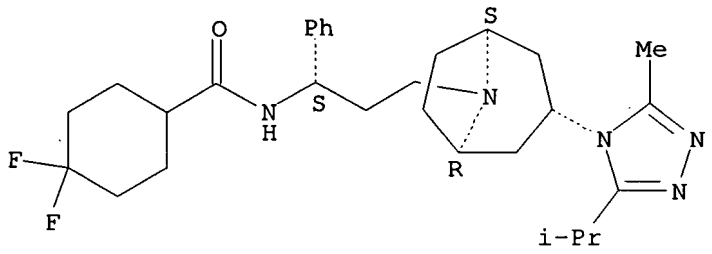
AB The title compds. I [x, y = 0-2; R = H, alkyl, haloalkyl, etc.; n = 0-3; R1 = halo, haloalkyl, alkyl, etc.; A = heteroaryl; R4 = halo, haloalkyl, alkyl, etc.; m = 0-2; p = 0-1; B = O, CO, CO2, etc.; D = N(R10)2, (un)substituted 4-6 membered heterocyclyl or heteroaryl; R10 = H, alkyl, cycloalkyl, etc.], useful in the treatment of diseases and conditions caused by CXCR4, were prepared E.g., a multi-step synthesis of trans-II, starting from 6,7-dihydro-8(5H)-quinolinone and acrylonitrile, was given. Compound I were tested in the HIV-1 infectivity assay (IC50 of about 1 nM to about 50 μM). Pharmaceutical formulations containing compds. I alone or in combination with other therapeutic agents are also disclosed.

IT 376348-65-1, Maraviroc
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of heteroarylmethyl substituted octahydro-1,10-phenanthrolines and their analogs for treating diseases modulated by a chemokine receptor (CXCR4))

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 23 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:769177 CAPLUS
DOCUMENT NUMBER: 145:180928
TITLE: Human neutrophil α-defensin 4 inhibition of HIV-1
INVENTOR(S): Lu, Wuyuan; Cocchi, Fiorenza; Wu, Zhibin
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 7pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2006172945	A1	20060803	US 2006-347538		20060203
PRIORITY APPLN. INFO.:			US 2005-649873P	P	20050203

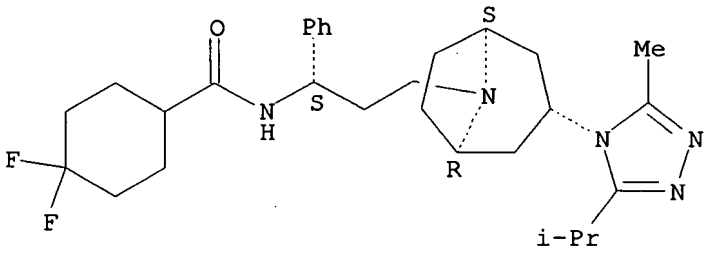
AB A method to reduce replication of HIV-1, involving administering a therapeutically effective amount of recombinant HNP4 to a subject in need thereof to combat HIV-1 infection. The HNP4 agent may be utilized in pharmaceutical compns. including a pharmaceutically acceptable carrier and an anti-viral agent, e.g., an anti-viral agent, or combination of such agents, such as nucleoside RT inhibitors, CCR5 inhibitors/antagonists, viral entry inhibitors, and functional analogs thereof.

IT 376348-65-1, UK 427857
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human neutrophil α-defensin 4 inhibition of HIV-1)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 24 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:722182 CAPLUS
DOCUMENT NUMBER: 145:262274
TITLE: CCR5 antagonists: the answer to inflammatory disease?
AUTHOR(S): Ness, Traci L.; Kunkel, Steven L.; Hogaboam, Cory M.
CORPORATE SOURCE: Department of Pathology, University of Michigan Medical School, Ann Arbor, MI, 48109-0602, USA
SOURCE: Expert Opinion on Therapeutic Patents (2006), 16(8), 1051-1065
CODEN: EOTPEG; ISSN: 1354-3776
PUBLISHER: Informa Healthcare
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Chemokines and their receptors mediate the inflammatory response during infectious and non-infectious disease. However, their continued activation and disregulation are commonly associated with chronic inflammation. Frequently, affected sites are characterised by inflammatory cell infiltrates expressing CC chemokine receptor 5 (CCR5) and high levels of CCR5 ligands. Neutralisation of CCR5 decreases the incidence and pathol. of these diseases in murine models, and epidemiol. studies in human patients corroborate these data. CCR5-deficiency has been associated with increased risk of hepatic disease and infection, but considering the pathol. effects of

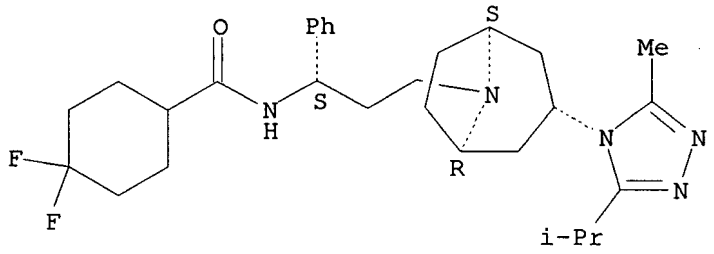
chronic inflammation, pharmacol. targeting CCR5 is still a desirable and feasible goal. The discovery that CCR5 is a major HIV coreceptor initiated the race to produce effective CCR5 antagonists. This review summarises the progress made in CCR5 antagonist development and assesses their potential in the treatment of inflammatory disease.

IT 376348-65-1, UK 427857
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CCR5 antagonists for inflammatory disease)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 157 THERE ARE 157 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 25 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:707184 CAPLUS
DOCUMENT NUMBER: 145:167247
TITLE: Preparation of N-[(imidazo[1,2-a]pyridin-2-yl)methyl]-3,4-dihydro-2H-pyrano[3,2-b]pyridin-4-amines that bind to chemokine receptors for use against HIV and other disorders
INVENTOR(S): Gudmundsson, Kristjan
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006076131	A2	20060720	WO 2005-US45994	20051216
WO 2006076131	A3	20060921		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,

KG, KZ, MD, RU, TJ, TM

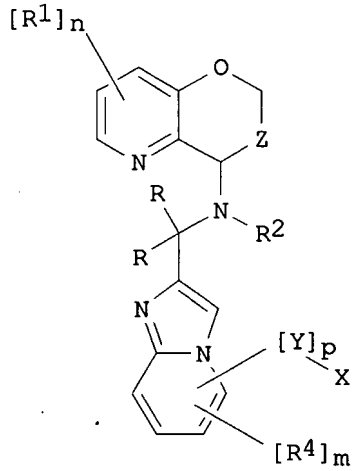
EP 1838312	A2	20071003	EP 2005-857134	20051216

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, HR

PRIORITY APPLN. INFO.: US 2004-636933P P 20041217
WO 2005-US45994 W 20051216

OTHER SOURCE(S): MARPAT 145:167247

GI



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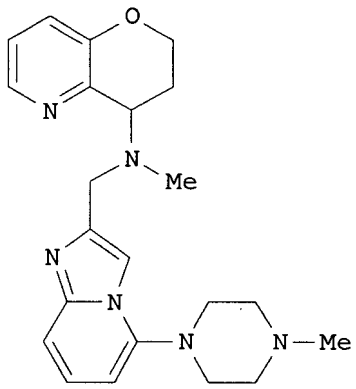


II

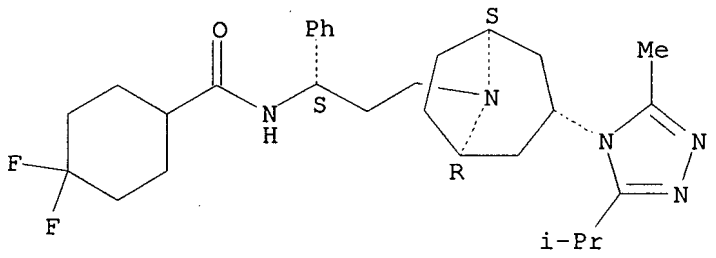
AB The invention is directed to the preparation of novel imidazo[1,2-a]pyridines I [Z = (CH2)q; q = 1-2; each R = independently H, alk(en/yn)yl, haloalkyl, etc.; each R1, each R4 = independently halo, CN, NO2, halo/cyclo/alkyl, alkenyl, OH and derivs., etc.; m, n = independently 0-2; R2 = H, halo/alkyl, alkenyl, etc.; p = 0-1; Y = NH and derivs., O, CONH, NHCO, COO, CO, SO, etc.; X = NH2 and derivs., (un)substituted heteroaryl, heterocyclyl, etc.] that demonstrate protective effects on target cells from HIV infection in a manner as to bind specifically to the chemokine receptor, and which affect the binding of the natural ligand or chemokine to a receptor such as CXCR4 and/or CCR5 of a target cell. For example, imidazopyridine II was prepared by reductive amination of 2,3-dihydro-4H-pyrano[3,2-b]pyridin-4-one with methylamine, and amination of the fluoride with N-methylpiperazine. Binding to the CXCR4 receptor, cytotoxicity towards the HOS cell line and the ability to block infection of the HOS cell line by 2 HIV-1 viruses by imidazopyridines I are tabulated.

IT 376348-65-1, UK 427857
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of imidazopyridines that bind to chemokine receptors for use against HIV and other disorders)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 26 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:676597 CAPLUS
DOCUMENT NUMBER: 145:117362
TITLE: Compositions for down-regulation of CCR5 expression and methods of use thereof
INVENTOR(S): Redfield, Robert R.; Amoroso, Anthony; Davis, Charles E.; Heredia, Alonso
PATENT ASSIGNEE(S): University of Maryland Biotechnology Institute, USA
SOURCE: U.S. Pat. Appl. Publ., 35 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006154857	A1	20060713	US 2005-281195	20051116
WO 2005001027	A2	20050106	WO 2004-US15681	20040517
WO 2005001027	A3	20060126		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-471453P P 20030516
WO 2004-US15681 A2 20040517

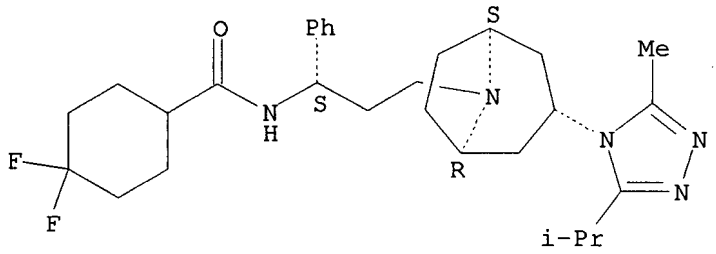
AB The present invention relates to the downregulation of surface receptor CCR5 expression through manipulation of the cell cycle in activated lymphocytes by administering a composition that arrests the G1 phase of the cell cycle, thereby reducing receptor sites for entry of HIV into T cells, and thus, the effects of HIV. Further, compns. are disclosed that include at least one G1 phase arresting agent and at least one antiviral agent, wherein the combination of agents synergistically enhances the activity of the antiviral agent.

IT 376348-65-1, UK 427857
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. for down-regulation of CCR5 expression by arresting G1 phase of cell cycle of activated lymphocytes and decreasing HIV virus entry and combination with other antiviral agents)

RN 376348-65-1 CAPLUS
CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-

phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 27 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:578211 CAPLUS
DOCUMENT NUMBER: 145:62897
TITLE: Preparation of spirotropane compounds and therapeutic use as modulators of chemokine receptor activity
INVENTOR(S): Chan Chun Kong, Laval; Moinet, Christophe; Courchesne, Marc; Vaillancourt, Louis; Blais, Charles; Bubenik, Monica
PATENT ASSIGNEE(S): Virochem Pharma Inc., Can.
SOURCE: PCT Int. Appl., 145 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006060919	A1	20060615	WO 2005-CA1878	20051209
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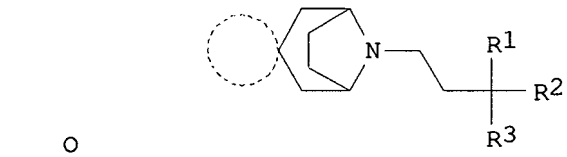
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2005313813	A1	20060615	AU 2005-313813	20051209
CA 2587508	A1	20060615	CA 2005-2587508	20051209
EP 1831222	A1	20070912	EP 2005-819431	20051209
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
IN 2007KN02150	A	20070817	IN 2007-KN2150	20070612

PRIORITY APPLN. INFO.:	US 2004-634266P	P	20041209
	US 2005-693051P	P	20050623
	WO 2005-CA1878	W	20051209

OTHER SOURCE(S): CASREACT 145:62897; MARPAT 145:62897
GI



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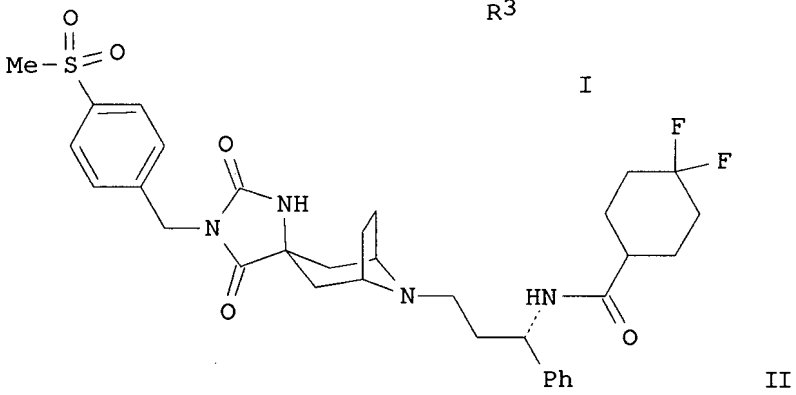


II

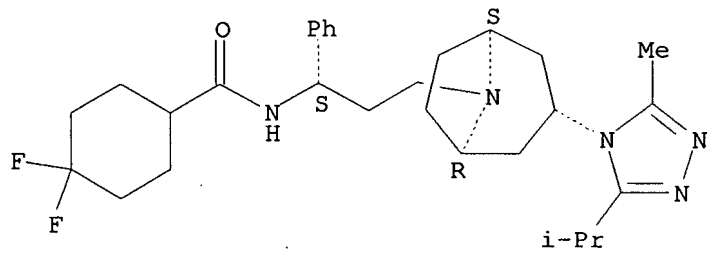
AB Spiro compds. according to formula (I) are claimed: wherein R1 = NR7R9; R2 = (un)substituted C1-10 alkyl, C2-10 alkenyl, 3-10 membered heterocycle, etc.; R3 = H, (un)substituted C1-10 alkyl or C6-12 aryl; R7 = H, (un)substituted C1-10 alkyl, C2-10 alkenyl, C2-10 alkynyl; R9 = H or (un)substituted C1-10-alkyl; and ring A represents a 5 or 6 membered heteroring substituted once or twice with a keto substituent. These compds. and their pharmaceutical acceptable salts are used in combinations or in pharmaceutical compns. and are useful in the modulation of CCR5 chemokine receptor activity (no data given). I are useful in the prevention or treatment of certain inflammatory diseases, immunoregulatory diseases, organ transplantation reactions and in the prevention and treatment of infectious diseases such as HIV infections. Preparation of I is exemplified. For example, II was prepared from
4,4-difluorocyclohexanecarboxylic acid ((S)-3-oxo-1-phenylpropyl)amide and 3-(4-methanesulfonylbenzyl)bicyclo[3.2.1]-1α,3,8-triazaspiro[4.5]dodecan-2,4-dione hydrochloride (preparation given).

IT 376348-65-1, UK 427857
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(addnl. therapeutic agent; preparation of spirotropane compds. and therapeutic use as modulators of chemokine receptor activity)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



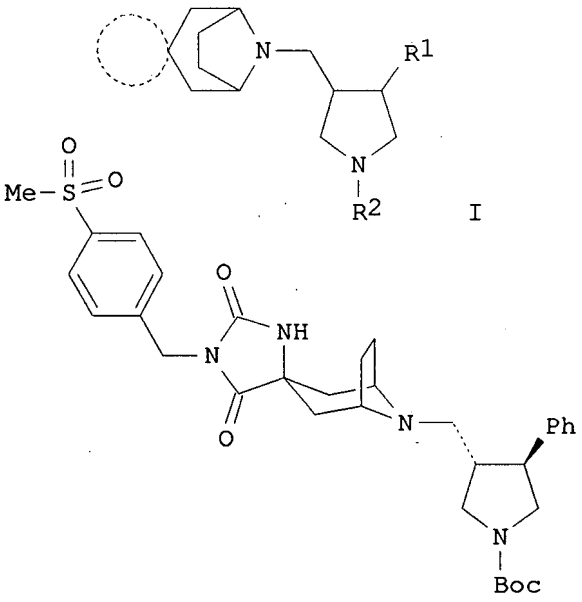
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 28 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:558325 CAPLUS
DOCUMENT NUMBER: 145:62894
TITLE: Preparation of spirotropane compounds and methods for the modulation of chemokine receptor activity to block cellular entry of HIV
INVENTOR(S): Chan Chun Kong, Laval; Moinet, Christophe; Courchesne, Marc; Vaillancourt, Louis; Bubenik, Monica
PATENT ASSIGNEE(S): Virochem Pharma Inc., Can.
SOURCE: PCT Int. Appl., 153 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006060918	A1	20060615	WO 2005-CA1877	20051209
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2590737	A1	20060615	CA 2005-2590737	20051209
EP 1824853	A1	20070829	EP 2005-819950	20051209
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				

PRIORITY APPLN. INFO.: US 2004-634257P P 20041209
WO 2005-CA1877 W 20051209

OTHER SOURCE(S): MARPAT 145:62894
GI



I

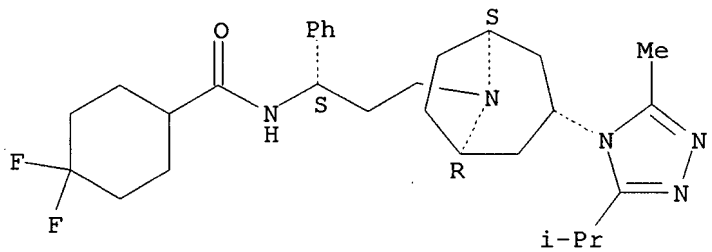
AB Compds. according to formula I (wherein the R1= (un)substituted alkyl, alkenyl, etc.; R2 = H, cycloalkylcarbonyl, ester, etc.; and A = a 5 or 6 membered heteroring involving a nitrogen or oxygen atom and one or two keto substituent) are claimed. These compds. and their pharmaceutical acceptable salt are used in combinations or pharmaceutical compns. and are useful in modulation of CCR5 chemokine receptor activity and blocking cellular entry of HIV (no biol. data given). Preparation of I is exemplified. For example, II was prepared from 3-(4-methanesulfonylbenzyl)bicyclo[3.2.1]-1a,3,8-triazaspiro[4.5]dodecan-2,4-dione hydrochloride (preparation given) and (3R,4S)-3-formyl-4-phenylpyrrolidine-1-carboxylic acid tert-Bu ester (preparation given).

IT 376348-65-1, UK 427857
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(addnl. therapeutic agent; preparation of spirotropane compds. and methods for modulation of chemokine receptor activity to block cellular entry of HIV)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

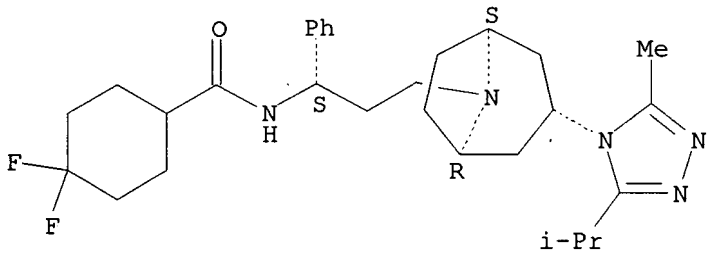
L6 ANSWER 29 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:536919 CAPLUS
DOCUMENT NUMBER: 145:448545
TITLE: A Pharmacokinetic-Pharmacodynamic Model to Optimize the Phase IIa Development Program of Maraviroc
AUTHOR(S): Rosario, Maria C.; Poland, Bill; Sullivan, John; Westby, Mike; van der Ryst, Elna
CORPORATE SOURCE: Dep. of Clinical Pharmacology, Pfizer Clinical R&D, Groton, CT, 06340, USA
SOURCE: JAIDS, Journal of Acquired Immune Deficiency Syndromes (2006), 42(2), 183-191
CODEN: JJASFJ; ISSN: 1525-4135
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Objectives: To use a viral dynamics model to compare the effectiveness of in vivo viral inhibition of several doses of maraviroc (MVC;UK-427,857) and to use a modeling approach to support design decisions for a monotherapy study using various dosing regimens of maraviroc given with and without food. Design: The pharmacokinetic-pharmacodynamic model was developed using clin. data from a first monotherapy study (study A4001007). This was a randomized, double-blind, placebo-controlled, multicenter study of maraviroc in 44 asymptomatic HIV-1-infected patients. Patients received maraviroc under food restrictions at 25 mg once daily or 50, 100, or 300 mg twice daily, or placebo for 10 days. Methods: Antiviral responses were assessed by measuring plasma HIV -1 RNA levels during screening, during randomization, at baseline, and daily during the 10 days of treatment and at days 11 to 15, 19, 22, 25, and 40. An integrated pharmacokinetic-pharmacodynamic model was developed using the mixed effects modeling approach with patients' pharmacokinetic profiles on the last day of treatment, HIV-1 RNA levels over time, and the individual viral susceptibility. The parameters derived from the viral dynamic model were used to calculate average viral inhibition fraction, decay rate of actively infected cells, and basic reproductive ratio for each treatment group. Monte Carlo simulation was then used to determine the distribution of viral load change across simulated patients over time for each regimen to be studied in another monotherapy study, A4001015. Results: The decline rate in the 300 mg twice daily group was comparable to that induced by potent protease inhibitor monotherapy, but was significantly slower than that in patients receiving combination therapy including both protease inhibitor and reverse transcriptase inhibitors. The efficacy of inhibition in vivo was estimated to range from 0.15 to 0.38 for the 25 mg once daily dose group and from 0.88 to 0.96 for the 300 mg twice daily dose group. Conclusions: The model has aided the anal. and interpretation of the clin. data. The use of a model-based approach for selecting doses can accelerate drug development by replacing some arms or trials with simulations.

IT 376348-65-1, Maraviroc
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacokinetic-pharmacodynamic model predicted revealed that impact of food on viral load would be attenuated with reduction of 14% in mean viral load decline with food innate in maraviroc treated HIV -1 infected patient)

RN 376348-65-1 CAPLUS
CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 30 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:474269 CAPLUS
DOCUMENT NUMBER: 144:480472
TITLE: Emergence of CXCR4-using human immunodeficiency virus type 1 (HIV-1) variants in a minority of HIV-1-infected patients following treatment with the CCR5 antagonist maraviroc is from a pretreatment CXCR4-using virus reservoir
AUTHOR(S): Westby, Mike; Lewis, Marilyn; Whitcomb, Jeannette; Youle, Mike; Pozniak, Anton L.; James, Ian T.; Jenkins, Tim M.; Perros, Manos; van der Ryst, Elna
CORPORATE SOURCE: Pfizer Global Research and Development, Sandwich, UK
SOURCE: Journal of Virology (2006), 80(10), 4909-4920
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Antagonists of the human immunodeficiency virus type 1 (HIV-1) coreceptor, CCR5, are being developed as the first anti-HIV agents acting on a host cell target. We monitored the coreceptor tropism of circulating virus, screened at baseline for coreceptor tropism, in 64 HIV-1-infected patients who received maraviroc (MVC, UK-427,857) as monotherapy for 10 days. Sixty-two patients harbored CCR5-tropic virus at baseline and had a posttreatment phenotype result. Circulating virus remained CCR5 tropic in 60/62 patients, 51 of whom experienced an HIV RNA reduction from baseline of > 1 log10 copies/mL, indicating that CXCR4-using variants were not rapidly selected despite CCR5-specific drug pressure. In two patients, viral load declined during treatment and CXCR4-using virus was detected at day 11. No pretreatment factor predicted the emergence of CXCR4-tropic virus during maraviroc therapy in these two patients. Phylogenetic anal. of envelope (Env) clones from pre- and posttreatment time points indicated that the CXCR4-using variants probably emerged by outgrowth of a pretreatment CXCR4-using reservoir, rather than via coreceptor switch of a CCR5-tropic clone under selection pressure from maraviroc. Phylogenetic anal. was also performed on Env clones from a third patient harboring CXCR4-using virus prior to treatment. This patient was enrolled due to a sample labeling error. Although this patient experienced no overall reduction in viral load in response to treatment, the CCR5-tropic components of the circulating virus did appear to be suppressed while receiving maraviroc as monotherapy. Importantly, in all three patients, circulating virus reverted to predominantly CCR5 tropic following cessation of maraviroc.

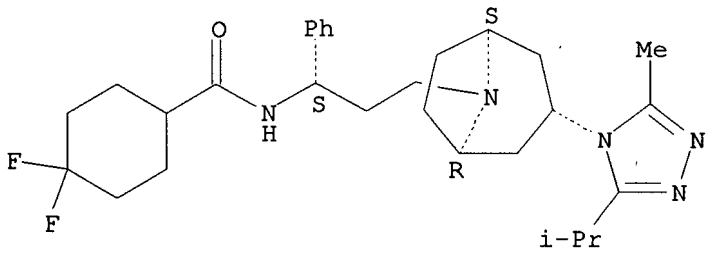
IT 376348-65-1, Maraviroc
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(emergence of CXCR4-using human immunodeficiency virus type 1 (

HIV-1) variants in minority of HIV-1-infected patients following treatment with CCR5 antagonist maraviroc is from pretreatment CXCR4-using virus reservoir)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 31 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:319029 CAPLUS

DOCUMENT NUMBER: 144:370090

TITLE: Aminotetrahydroquinolines as cytoprotectants from HIV infection, their preparation, pharmaceutical compositions, and use in therapy

INVENTOR(S): Gudmundsson, Kristjan; Boggs, Sharon Davis

PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA

SOURCE: PCT Int. Appl., 118 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006036816	A2	20060406	WO 2005-US34218	20050923
WO 2006036816	A3	20060615		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1793825	A2	20070613	EP 2005-817347	20050923
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, HR				

PRIORITY APPLN. INFO.: US 2004-612844P P 20040924
WO 2005-US34218 W 20050923

OTHER SOURCE(S): MARPAT 144:370090

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

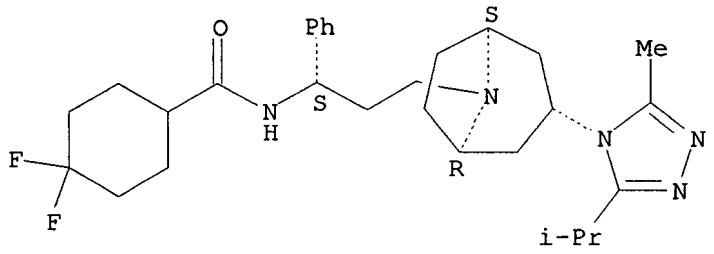
AB The invention relates to compds. of general formula I, which demonstrate protective effects on target cells from HIV infection in a manner as to bind specifically to the chemokine receptor, and which affect the binding of the natural ligand or chemokine to a receptor such as CXCR4 and/or CCR5 of a target cell. In compds. I, p is 0-2; each R1 is independently selected from halo, alkyl, haloalkyl, alkenyl, cycloalkyl, (un)substituted aryl, (un)substituted heteroaryl, (un)substituted heterocyclyl, etc.; n is 0-2; each R2 is independently selected from H, alkyl, alkenyl, alkynyl, haloalkyl, cycloalkyl, etc.; R3 is selected from H, halo, alkyl, haloalkyl, cycloalkyl, alkenyl, alkynyl, etc.; each R4 is independently selected from halo, cyano, nitro, alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, (un)substituted aryl, (un)substituted heteroaryl, (un)substituted heterocyclyl, etc.; m is 0-2; Y is (un)substituted alkylene, (un)substituted cycloalkylene, alkenylene, cycloalkenylene, or alkynylene; and Z is (un)substituted amino, (un)substituted aminoaryl, (un)substituted heteroaryl, (un)substituted heterocyclyl, etc.; including pharmaceutically acceptable salts and esters thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a compound I and a pharmaceutically acceptable carrier, optionally containing one or more addnl. therapeutic agents, as well as to the use of the compns. for the prevention of infection of a cell by HIV. Reductive amination of quinolinone II with tert-Bu N-(4-aminobutyl)carbamate and reductive amination with 5-fluoroimidazo[1,2-a]pyridine-2-carboxaldehyde gave amine III, which underwent substitution with tert-Bu piperazine-1-carboxylate and deprotection to give aminotetrahydroquinoline IV. Several compds. of the invention show HIV anti-infective activity, e.g., compound IV expresses activity of 2.2 nM in an HOS HIV-1 anti-infectivity assay.

IT 376348-65-1, UK 427857
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of aminotetrahydroquinolines as cytoprotectants from HIV infection)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 32 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:254138 CAPLUS
DOCUMENT NUMBER: 145:201842
TITLE: Development of a novel dual CCR5-dependent and CXCR4-dependent cell-cell fusion assay system with

inducible gp160 expression

AUTHOR(S): Ji, Changhua; Zhang, Jun; Cammack, Nick; Sankuratri, Surya

CORPORATE SOURCE: Viral Diseases, Roche Palo Alto, Palo Alto, CA, USA

SOURCE: Journal of Biomolecular Screening (2006), 11(1), 65-74
CODEN: JBISF3; ISSN: 1087-0571

PUBLISHER: Sage Publications

DOCUMENT TYPE: Journal

LANGUAGE: English

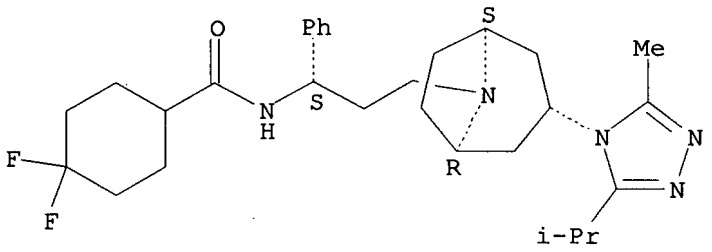
AB In the current study, a novel coreceptor-specific cell-cell fusion (CCF) assay system is reported. The system possesses the following features: dual CCR5-dependent and CXCR4-dependent CCF assays, all stable cell lines, inducible expression of gp160 to minimize cytotoxicity, robust luciferase reporter, and 384-well format. These assays have been validated using various known HIV entry inhibitors targeting various stages of the HIV entry/fusion process, including fusion inhibitors, gp120 inhibitors, CCR5 antagonists, CCR5 antibodies, and CXCR4 antagonists. IC50 data generated from this assay system were well correlated to that from the antiviral assays. The effects of DMSO on this assay system were assessed, and a 2- to 3-fold increase in luciferase activity was observed in the presence of 0.05% to 2% DMSO. Although cell-cell fusion efficiency was enhanced, no changes in drug response kinetics for entry inhibitors were found in the presence of 0.1% or 0.5% DMSO. This assay system has been successfully used for the identification and characterization of thousands of CCR5 inhibitors.

IT 376348-65-1, UK 427857
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(UK427,857 inhibited CCR5-dependent cell-cell fusion assays in HeLa-R5 and HeLa-X4 cell lines)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 33 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:232041 CAPLUS

DOCUMENT NUMBER: 144:305114

TITLE: Methods of treating HIV infection

INVENTOR(S): Krystal, Mark; Deminie, Carol A.; Bollini, Sagarika; Terry, Brian J.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 12 pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006058286	A1	20060316	US 2005-227526	20050915
WO 2006034001	A2	20060330	WO 2005-US33048	20050916
WO 2006034001	A3	20061123		

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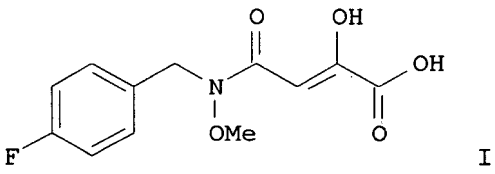
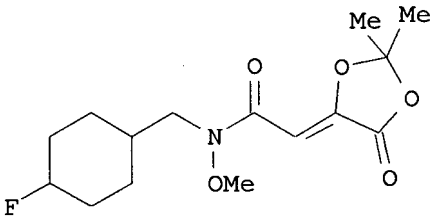
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2004-610343P P 20040916

GI



I



II

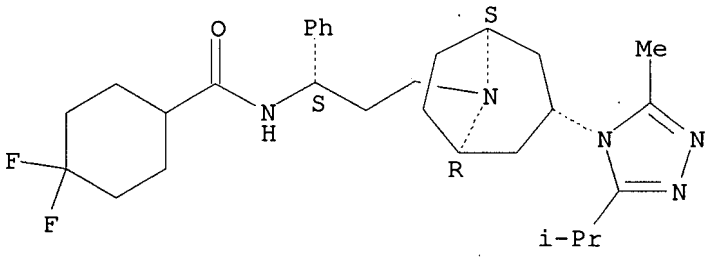
AB The invention encompasses pharmaceutical compns. (I and II) and methods for using I or II in combination with other agents for treating patients with AIDS or HIV infection.

IT 376348-65-1, UK 427857
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods of treating HIV infection)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 34 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:212428 CAPLUS
DOCUMENT NUMBER: 144:274277
TITLE: Preparation of imidazo[1,2-a]pyridine derivatives as chemokine receptor ligands with anti-HIV activity
INVENTOR(S): Gudmundsson, Kristjan; Boggs, Sharon Davis
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 184 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006026703	A2	20060309	WO 2005-US31099	20050831
WO 2006026703	A3	20061005		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1799671	A2	20070627	EP 2005-815072	20050828
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, HR				
AU 2005279835	A1	20060309	AU 2005-279835	20050831
CA 2578746	A1	20060309	CA 2005-2578746	20050831
AU 2005282753	A1	20060316	AU 2005-282753	20050831
CA 2579059	A1	20060316	CA 2005-2579059	20050831
WO 2006028896	A2	20060316	WO 2005-US31098	20050831
WO 2006028896	A3	20060427		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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EP 1784185	A2	20070516	EP 2005-794929		20050831
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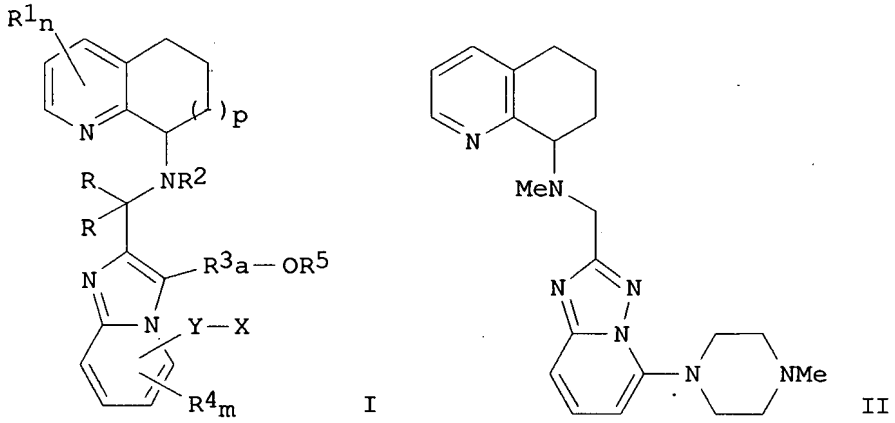
CN 101052399	A	20071010	CN 2005-80037876		20050831
CN 101052635	A	20071010	CN 2005-80037993		20050831
IN 2007KN00701	A	20070713	IN 2007-KN701		20070226
US 2007232615	A1	20071004	US 2007-574583		20070302
IN 2007KN00823	A	20070713	IN 2007-KN823		20070307
NO 2007001366	A	20070531	NO 2007-1366		20070314
NO 2007001418	A	20070531	NO 2007-1418		20070315
PRIORITY APPLN. INFO.:			US 2004-606742P	P	20040902
			US 2004-610765P	P	20040917
			WO 2005-US31098	W	20050831
			WO 2005-US31099	W	20050831

OTHER SOURCE(S): MARPAT 144:274277

GI



I II

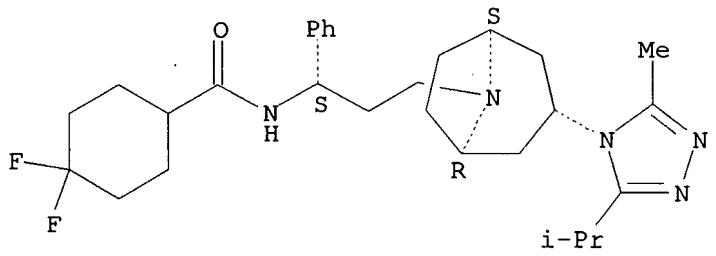
AB Title compds. represented by the formula I [wherein p = 0-2; R = independently H, (halo)alkyl, alkenyl, etc.; R1, R4 = independently halo, (halo)alkyl, alkynyl, etc.; n = 0-2; m = 0-2; R2 = H, (cyclo)alkyl, alkenyl, etc.; R3 = independently (cyclo)alkylene, oxo, hydroxy, etc.; a = 0 or 1; R5 = independently H, (cyclo)alkyl, alkenyl, alkynyl or (un)substituted aryl; Y = (un)substituted amino, O, CO, etc.; X = (un)substituted amino, arylamino, heterocyclyl, etc.; and pharmaceutically acceptable salts or esters thereof] were prepared as chemokine receptor ligands with anti-HIV activity. For example, microwave irradiation of N-[(5-fluoroimidazo[1,2-a]pyridin-2-yl)methyl]-N-methyl-5,6,7,8-tetrahydro-8-quinolinamine (preparation given) and 1-methylpiperazine in 67% yield. In infectivity assays, I demonstrated activity in the range of less than 100 nM up to 10 μM. The present invention provides novel compds. that demonstrate protective effects on target cells from HIV infection in a manner as to bind specifically to the chemokine receptor, and which affect the binding of the natural ligand or chemokine to a receptor such as CXCR4 and/or CCR5 of a target cell.

IT 376348-65-1, UK 427857
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of (quinolinylaminoalkyl)-imidazopyridine derivs. as chemokine receptor ligands)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 35 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:193595 CAPLUS
DOCUMENT NUMBER: 144:274272
TITLE: Preparation of (quinolinylaminoalkyl)-benzimidazole derivatives as chemokine receptor ligands with anti-HIV activity
INVENTOR(S): Gudmundsson, Kristjan; Sebahar, Paul Richard; Richardson, Leah D'Aurora
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 303 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006023400	A2	20060302	WO 2005-US28811	20050812
WO 2006023400	A3	20060608		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2005277638	A1	20060302	AU 2005-277638	20050812
CA 2577100	A1	20060302	CA 2005-2577100	20050812
EP 1789045	A2	20070530	EP 2005-786708	20050812
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, HR				
CN 101039672	A	20070919	CN 2005-80035165	20050812
IN 2007KN00685	A	20070706	IN 2007-KN685	20070223
KR 2007042568	A	20070423	KR 2007-705000	20070228
NO 2007001161	A	20070514	NO 2007-1161	20070301

PRIORITY APPLN. INFO.: US 2004-601928P P 20040816
WO 2005-US28811 W 20050812
OTHER SOURCE(S): CASREACT 144:274272; MARPAT 144:274272
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

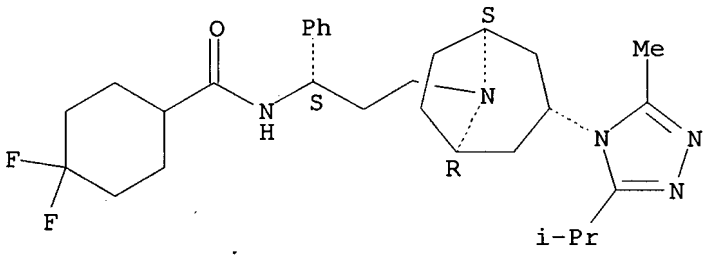
AB Title compds. I [X = (CH2)q where q = 0-2; each R independently = H, alkyl, alkenyl, haloalkyl, etc.; R1 = halo, alkyl, cycloalkyl, etc.; R2 = H, (un)substituted alkyl, alkenyl, etc.; R3 = H, (un)substituted alkyl, haloalkyl, alkynyl, etc.; R4 independently = halo, alkenyl, alkynyl, etc.; R5 = (un)substituted amine, aminoaryl, aminoheterocyclyl, etc.; n = 0-2; m = 0-2; p = 0-1], and their pharmaceutically acceptable salts, are prepared and disclosed as demonstrating protective effects on target cells from HIV infection in a manner as to bind specifically to the chemokine receptor, and which affect the binding of the natural ligand or chemokine to a receptor such as CXCR4 and/or CCR5 of a target cell. Thus, e.g. II, was prepared by hydrolysis of Me 1-methyl-2-{[methyl-(5,6,7,8-tetrahydro-8-quinolinyl)amino]methyl}-1H-benzimidazole-7-carboxylate (preparation given) followed by coupling with histamine. In infectivity assays, I demonstrated activity in the range of less than 100 nM up to 10 μM. Pharmaceutical compns. are disclosed.

IT 376348-65-1, UK 427857
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of (quinolinylaminoalkyl)-benzimidazole derivs. as chemokine receptor ligands)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

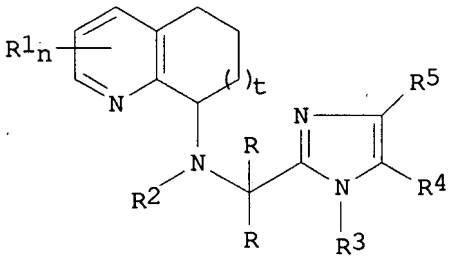
Absolute stereochemistry.



L6 ANSWER 36 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:164536 CAPLUS
DOCUMENT NUMBER: 144:233072
TITLE: Preparation of 8-(imidazol-2-ylmethylamino)-5,6,7,8-tetrahydroquinolines that bind to chemokine receptors for use against HIV and other disorders
INVENTOR(S): Gudmundsson, Kristjan; Miller, John Franklin; Turner, Elizabeth Madalena
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 272 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2006020415 A1 20060223 WO 2005-US26797 20050729
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
CA 2575560 A1 20060223 CA 2005-2575560 20050729
EP 1778231 A1 20070502 EP 2005-776484 20050729
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, HR
PRIORITY APPLN. INFO.: US 2004-598030P P 20040802
WO 2005-US26797 W 20050729
OTHER SOURCE(S): MARPAT 144:233072
GI



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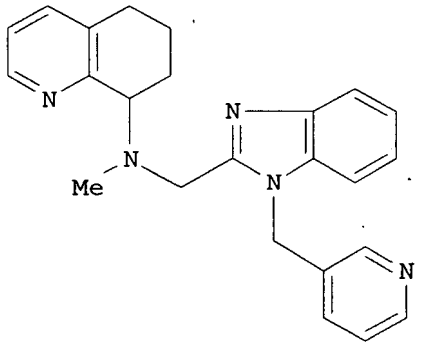


II

AB The present invention provides novel 8-(imidazol-2-ylmethylamino)-5,6,7,8-tetrahydroquinolines (shown as I; variables defined below; e.g. N-methyl-N-[[1-[(3-pyridinyl)methyl]-1H-benzimidazol-2-yl]methyl]-5,6,7,8-tetrahydro-8-quinolinamine (shown as II)) that demonstrate protective effects on target cells from HIV infection in a manner as to bind specifically to the chemokine receptor, and which affect the binding of the natural ligand or chemokine to a receptor such as CXCR4 and/or CCR5 of a target cell. For I: t = 0-2; each R independently is H, alkyl, alkenyl, alkynyl, haloalkyl, cycloalkyl, -RaAy, -RaOR10, or -RaS(O)mR10; each R1 independently is halogen, haloalkyl, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, -Ay, -NHAy, -Het, -NHHet, -OR10, -OAy, -OHet, -RaOR10, -NR6R7, -RaNR6R7, -RaC(O)R10, -C(O)R10, -CO2R10, -RaCO2R10, -C(O)NR6R7, -C(O)Ay, - C(O)Het, -S(O)2NR6R7, -S(O)mR10,

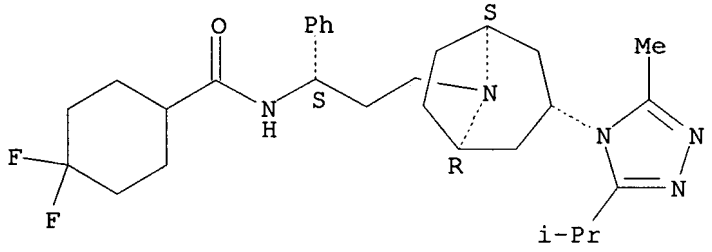
-S(O)mAy, cyano, nitro, or azido; n = 0-2; each m independently = 0-2; each R2 independently is H, alkyl, alkenyl, alkynyl, haloalkyl, cycloalkyl, -RaAy, - RaOR10, or -RaS(O)mR10 wherein R2 is not amine or alkylamine, or substituted with amine or alkylamine. R3 is -Het where Het is (un)substituted, -RaHet where Het is (un)substituted, -RaNR6R7, -Ay[NR6R7]p, -RaAy[NR6R7]p, -Ay[RaNR6R7]p, -RaAy[RaNR6R7]p, -Het[NR6R7]p, -RaHet[NR6R7]p, -Het[RaNR6R7]p, or RaHet[RaNR6R7]p; each p independently = 1-2; each of R4 and R5 independently = H, alkyl, alkenyl, alkynyl, cycloalkyl, -Ay, -Het, -RaAy, -RaHet, -OR10, -NR6R7, -RaNR6R7, -C(O)R10, -CO2R10 -C(O)NR6R7, -S(O)2NR6R7, -S(O)mR10, cyano, nitro, or azido. Or R4 and R5 may combine to form a ring containing ≥1 degrees of unsatn. that is fused with the depicted imidazole ring (un)substituted with (R1)n; each of R6 and R7 independently = H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, -Racycloalkyl, -RaOH, -RaOR10, -RaNRSR9, -Ay, -Het, -RaAy, -RaHet, or S(O)mR10; each of R8 and R9 independently = H or alkyl; each R10 independently is H, alkyl, alkenyl, alkynyl, cycloalkyl, or -Ay; each Ra independently is alkylene, cycloalkylene, alkenylene, cycloalkenylene, or alkynylene; and each Ay = an (un)substituted aryl group; and each Het = an (un)substituted 4-, 5-, or 6-membered heterocyclyl or heteroaryl group. Methods of preparation are claimed and prepns. and/or characterization data for .apprx.110 examples of I are included. For example, II was prepared in 3 steps (74, 82, 66 %) starting condensation of 6,7-dihydro-8(5H)-quinolinone with 2-(aminomethyl)benzimidazole dihydrochloride with subsequent reduction to N-[(1H-benzimidazol-2-yl)methyl]-5,6,7,8-tetrahydro-8-quinolinamine, which was N-methylated using formaldehyde/HOAc/NaBH(OAc)3 to give N-[(1H-benzimidazol-2-yl)methyl]-N-methyl-5,6,7,8-tetrahydro-8-quinolinamine, which was N-alkylated by 3-(chloromethyl)pyridine hydrochloride. Binding to the CXCR4 receptor, cytotoxicity towards the HOS cell line and the ability to block infection of the HOS cell line by 2 HIV-1 viruses by many examples of I are tabulated.

IT 376348-65-1, UK 427857
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of 8-(imidazol-2-ylmethylamino)-5,6,7,8-tetrahydroquinolines that bind to chemokine receptors for use against HIV and other disorders)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 37 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:13921 CAPLUS
DOCUMENT NUMBER: 144:83640
TITLE: Compositions and methods for determining resistance to inhibitors of virus entry using recombinant virus assays
INVENTOR(S): Petropoulos, Christos J.

PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 34 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006003319	A1	20060105	US 2005-146879	20050606
AU 2005264884	A1	20060126	AU 2005-264884	20050607
CA 2570975	A1	20060126	CA 2005-2570975	20050607
WO 2006009622	A1	20060126	WO 2005-US20240	20050607
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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1774049	A1	20070418	EP 2005-791148	20050607
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				

PRIORITY APPLN. INFO.: US 2004-577851P P 20040607
WO 2005-US20240 W 20050607

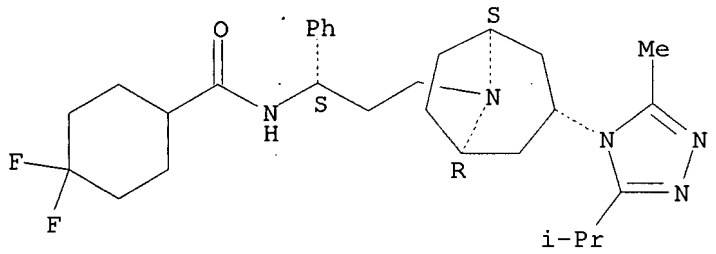
AB The invention provides a method for determining whether a human immunodeficiency virus is resistance to a viral entry inhibitor. The methods are particularly useful for determining resistance to inhibitors that act by a non-competitive mechanism. In certain aspects, the methods comprise determining whether an HIV population is resistant to an HIV entry inhibitor, comprising determining a log-sigmoid inhibition curve comprising data points for entry of the HIV population in the presence of varying concns. of the HIV entry inhibitor, wherein if the entry of the HIV population cannot be completely inhibited by the HIV entry inhibitor, the HIV population is resistant to the HIV entry inhibitor.

IT 376348-65-1, UK 427857
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as HIV virus entry inhibitor; determining drug resistance to inhibitors of virus entry using recombinant virus assays)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 38 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1276681 CAPLUS
DOCUMENT NUMBER: 144:304464
TITLE: A pharmacokinetic-pharmacodynamic disease model to predict in vivo antiviral activity of maraviroc
AUTHOR(S): Rosario, Maria C.; Jacqmin, Philippe; Dorr, Pat; van der Ryst, Elna; Hitchcock, Chris
CORPORATE SOURCE: Department of Clinical PK/PD, Pfizer Global Medical and Development Sciences, Groton, CT, USA
SOURCE: Clinical Pharmacology & Therapeutics (New York, NY, United States) (2005), 78(5), 508-519
CODEN: CLPTAT; ISSN: 0009-9236
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The viral dynamics of human immunodeficiency virus (HIV) infection has been widely studied and expressed as mathematic equations. For most of the current registered antiretroviral drugs, the pharmacokinetics is well characterized and some relationships with the viral load-time profiles in plasma from HIV patients have been established. The integration of these models in a pharmacokinetic (PK)-pharmacodynamic (PD)-disease model can help toward a better understanding of the complexity of the interactions, as well as in the identification and clarification of the current model assumptions. This work describes the development of a generic PK-PD disease model for a short-term (10 days) monotherapy phase IIa study with a novel anti-HIV drug, maraviroc (UK-427,857). The disease component of the model was based on the model published by Bonhoeffer et al, which was adapted for short-term treatment and for the new mechanism of action, CCR5-receptor antagonism. The model parameters were derived from the literature, as well as from a model-based anal. of available phase IIa clin. data from another investigational antiretroviral drug. The PD component that links the plasma concns. of maraviroc to the inhibition of virus replication was based on in vitro measurements of drug potency and took into account the difference in the in vitro and in vivo protein binding and the uncertainties regarding the interpretation of the in vitro to in vivo extrapolation of the 50% inhibitory concentration Finally, the PK component was based on information obtained from a single-dose study in healthy volunteers. The integrated PK-PD disease modeling allowed prediction of the effect on viral load of different maraviroc doses given as monotherapy to drug-naive patients. By making use of the available PK-PD disease model, the possible range of active oral doses for maraviroc in HIV-pos. patients was estimated by simulation before any clin. trials were taking place. The use of a model-based approach for selecting doses for clin. phase IIa has improved and accelerated the drug's development. This model was a powerful tool for assisting in the design of clin. studies on new agents for treating HIV/acquired immunodeficiency syndrome.

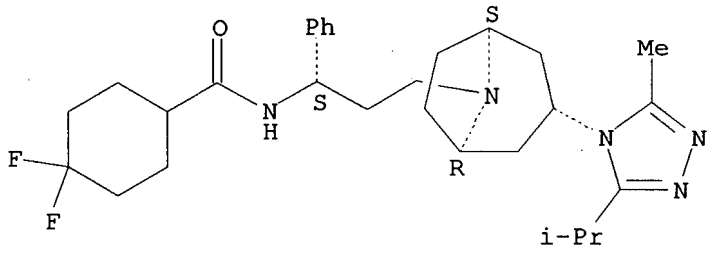
IT 376348-65-1, Maraviroc
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological

study); USES (Uses)
(phase II trial of pharmacokinetic-pharmacodynamic disease modeling showed monotherapy with different doses of maraviroc predicted decrease of viral load in HIV-1-infected patient with acquired immunodeficiency syndrome)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 39 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:1256967 CAPLUS

DOCUMENT NUMBER: 144:368023

TITLE: CCR5: a target for therapeutic intervention of HIV-1 infection

AUTHOR(S): Mitsuya, Hiroaki

CORPORATE SOURCE: Dep. of Infectious Diseases, Dep. of Hematology, School of Medicine, Kumamoto University, Japan

SOURCE: Jikken Igaku (2005), 23(17), 2726-2731
CODEN: JIIGEF; ISSN: 0288-5514

PUBLISHER: Yodosha

DOCUMENT TYPE: Journal; General Review

LANGUAGE: Japanese

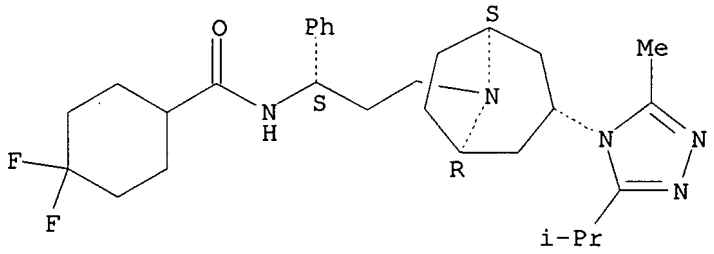
AB A review on human immunodeficiency virus-1 (HIV-1) invasion inhibitors and chemokine receptor antagonists, discussing (1) gp41 targeted inhibitors T-20 and T-1249 and CD4 binding inhibitors PRO542 and TNX-355 and anti-CXCR4 agents, (2) CCR5 antagonists maraviroc, aplaviroc, vicraviroc and TAK-652 and (3) structural anal. of CCR5 and CCR5 antagonist binding.

IT 376348-65-1, Maraviroc
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CCR5 as a target for therapeutic intervention of HIV -1 infection)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 40 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1201940 CAPLUS
DOCUMENT NUMBER: 143:432085
TITLE: Maraviroc (UK-427,857), a potent, orally bioavailable, and selective small-molecule inhibitor of chemokine receptor CCR5 with broad-spectrum anti-human immunodeficiency virus type 1 activity
AUTHOR(S): Dorr, Patrick; Westby, Mike; Dobbs, Susan; Griffin, Paul; Irvine, Becky; Macartney, Malcolm; Mori, Julie; Rickett, Graham; Smith-Burchnell, Caroline; Napier, Carolyn; Webster, Rob; Armour, Duncan; Price, David; Stammen, Blanda; Wood, Anthony; Perros, Manos
CORPORATE SOURCE: Pfizer Global Research and Development-Sandwich Laboratories, Sandwich, Kent, CT13 9NJ, UK
SOURCE: Antimicrobial Agents and Chemotherapy (2005), 49(11), 4721-4732
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Maraviroc (UK-427,857) is a selective CCR5 antagonist with potent antihuman immunodeficiency virus type 1 (HIV-1) activity and favorable pharmacol. properties. Maraviroc is the product of a medicinal chemical effort initiated following identification of an imidazopyridine CCR5 ligand from a high-throughput screen of the Pfizer compound file. Maraviroc demonstrated potent antiviral activity against all CCR5-tropic HIV-1 viruses tested, including 43 primary isolates from various clades and diverse geog. origin (geometric mean 90% inhibitory concentration of 2.0 nM). Maraviroc was active against 200 clin. derived HIV-1 envelope-recombinant pseudoviruses, 100 of which were derived from viruses resistant to existing drug classes. There was little difference in the sensitivity of the 200 viruses to maraviroc, as illustrated by the biol. cutoff in this assay (= geometric mean plus two standard deviations [SD] of 1.7-fold). The mechanism of action of maraviroc was established using cell-based assays, where it blocked binding of viral envelope, gp120, to CCR5 to prevent the membrane fusion events necessary for viral entry. Maraviroc did not affect CCR5 cell surface levels or associated intracellular signaling, confirming it as a functional antagonist of CCR5. Maraviroc has no detectable in vitro cytotoxicity and is highly selective for CCR5, as confirmed against a wide range of receptors and enzymes, including the hERG ion channel (50% inhibitory concentration, > 10 μM), indicating potential for an excellent clin. safety profile. Studies in preclin. in vitro and in vivo models predicted maraviroc to have human pharmacokinetics consistent with once- or twice-daily dosing following oral administration. Clin. trials are ongoing to further investigate the potential of using maraviroc for the treatment of HIV-1 infection and AIDS.

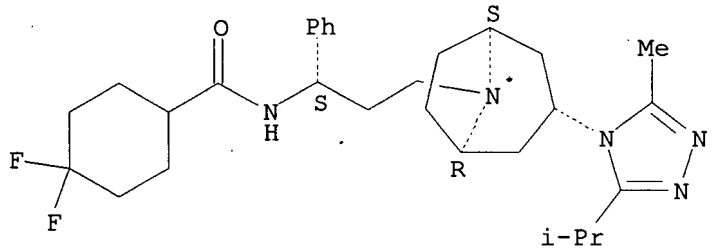
IT 376348-65-1, Maraviroc
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU

(Therapeutic use); BIOL (Biological study); USES (Uses)
(maraviroc (UK-427,857), a potent, orally bioavailable, and selective small-mol. inhibitor of chemokine receptor CCR5 with broad-spectrum anti-human immunodeficiency virus type 1 activity)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 41 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:1172256 CAPLUS

DOCUMENT NUMBER: 143:432076

TITLE: Efficacy of short-term monotherapy with maraviroc, a new CCR5 antagonist, in patients infected with HIV-1

AUTHOR(S): Faetkenheuer, Gerd; Pozniak, Anton L.; Johnson, Margaret A.; Plettenberg, Andreas; Staszewski, Schlomo; Hoepelman, Andy I. M.; Saag, Michael S.; Goebel, Frank D.; Rockstroh, Juergen K.; Dezube, Bruce J.; Jenkins, Tim M.; Medhurst, Christine; Sullivan, John F.; Ridgway, Caroline; Abel, Samantha; James, Ian T.; Youle, Mike; van der Ryst, Elna

CORPORATE SOURCE: Department of Internal Medicine, Division of Infectious Diseases, University of Cologne, Cologne, D-50924, Germany

SOURCE: Nature Medicine (New York, NY, United States) (2005), 11(11), 1170-1172
CODEN: NAMEFI; ISSN: 1078-8956

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

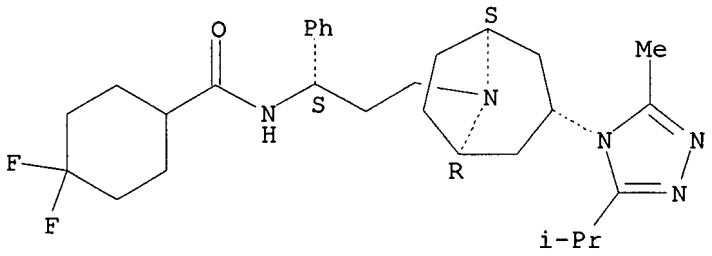
AB We assessed the efficacy and safety of 10-d monotherapy with the orally administered CCR5 antagonist maraviroc in 63 HIV-1-pos. individuals prescreened for the absence of CXCR4-using virus. Maximum reduction in viral load occurred at a median of 10-15 d, with a mean reduction of ≥1.6 log10copies/mL at all twice daily doses ≥100 mg. These results provide proof of concept that CCR5 antagonism is a viable antiretroviral therapeutic approach.

IT 376348-65-1, Maraviroc
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(efficacy of short-term monotherapy with maraviroc, a new CCR5 antagonist, in patients infected with HIV-1)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 42 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1131007 CAPLUS
DOCUMENT NUMBER: 144:141709
TITLE: Emerging drug targets for antiretroviral therapy
AUTHOR(S): Reeves, Jacqueline D.; Piefer, Andrew J.
CORPORATE SOURCE: Department of Microbiology, University of Pennsylvania, Philadelphia, PA, USA
SOURCE: Drugs (2005), 65(13), 1747-1766
CODEN: DRUGAY; ISSN: 0012-6667
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Current targets for antiretroviral therapy (ART) include the viral enzymes reverse transcriptase and protease. The use of a combination of inhibitors targeting these enzymes can reduce viral load for a prolonged period and delay disease progression. However, complications of ART, including the emergence of viruses resistant to current drugs, are driving the development of new antiretroviral agents targeting not only the reverse transcriptase and protease enzymes but novel targets as well. Indeed, enfuvirtide, an inhibitor targeting the viral envelope protein (Env) was recently approved for use in combination therapy in individuals not responding to current antiretroviral regimens. Emerging drug targets for ART include: (i) inhibitors that directly or indirectly target Env; (ii) the HIV enzyme integrase; and (iii) inhibitors of maturation that target the substrate of the protease enzyme. Env mediates entry of HIV into target cells via a multistep process that presents three distinct targets for inhibition by viral and cellular-specific agents. First, attachment of virions to the cell surface via nonspecific interactions and CD4 binding can be blocked by inhibitors that include cyanovirin-N, cyclotriazadisulfonamide analogs, PRO 2000, TNX 355 and PRO 542. In addition, BMS 806 can block CD4-induced conformational changes. Secondly, Env interactions with the co-receptor mols. can be targeted by CCR5 antagonists including SCH-D, maraviroc (UK 427857) and aplaviroc (GW 873140), and the CXCR4 antagonist AMD 070. Thirdly, fusion of viral and cellular membranes can be inhibited by peptides such as enfuvirtide and tifuvirtide (T 1249). The development of entry inhibitors has been rapid, with an increasing number entering clin. trials. Moreover, some entry inhibitors are also being evaluated as candidate microbicides to prevent mucosal transmission of HIV. The integrase enzyme facilitates the integration of viral DNA into the host cell genome. The uniqueness and specificity of this reaction makes integrase an attractive drug target. However, integrase inhibitors have been slow to reach clin. development, although recent contenders, including L 870810, show promise. Inhibitors that target viral maturation via a unique mode of action, such as PA 457, also have potential. In addition, recent advances in our understanding of cellular pathways involved

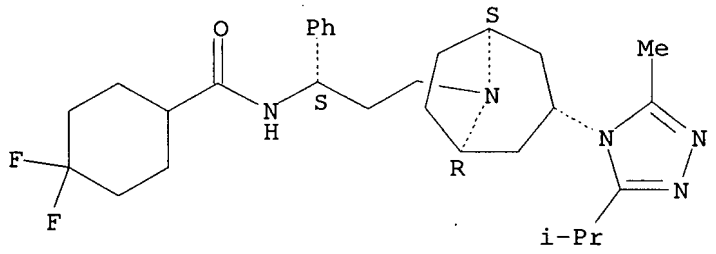
in the life cycle of HIV have also identified novel targets that may have potential for future antiretroviral intervention, including interactions between the cellular proteins APOBEC3G and TSG101, and the viral proteins Vif and p6, resp. In summary, a number of antiretroviral agents in development make HIV entry, integration and maturation emerging drug targets. A multifaceted approach to ART, using combinations of inhibitors that target different steps of the viral life cycle, has the best potential for long-term control of HIV infection. Furthermore, the development of microbicides targeting HIV holds promise for reducing HIV transmission events.

IT 376348-65-1, Maraviroc
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CCR5 antagonist maraviroc showed potential in therapy of human immunodeficiency virus infected patient through targeting Env interactions with co-receptor mols.)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 222 THERE ARE 222 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 43 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1050856 CAPLUS
DOCUMENT NUMBER: 143:319114
TITLE: Methods using a combination of 1-benzoyl-4-[2-[4-methoxy-7-(3-methyl-1H-1,2,4-triazol-1-yl)-1H-pyrrolo[2,3-c]pyridin-3-yl]-1,2-dioxoethyl]-piperazine and another anti-HIV agent for treating HIV infection
INVENTOR(S): Lin, Pin-Fang; Nowicka-Sans, Beata; Yamanaka, Gregory
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 14 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005215545	A1	20050929	US 2005-64683	20050224
AU 2005235116	A1	20051103	AU 2005-235116	20050301
CA 2561146	A1	20051103	CA 2005-2561146	20050301
WO 2005102392	A2	20051103	WO 2005-US6277	20050301
WO 2005102392	A3	20060720		

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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1732604	A2	20061220	EP 2005-723932		20050301
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CN 1956720	A	20070502	CN 2005-80016066		20050301
BR 2005009140	A	20070904	BR 2005-9140		20050301
MX 2006PA10885	A	20061116	MX 2006-PA10885		20060922
KR 2007011322	A	20070124	KR 2006-719595		20060922
IN 2006DN05560	A	20070824	IN 2006-DN5560		20060925
NO 2006004547	A	20061006	NO 2006-4547		20061006
PRIORITY APPLN. INFO.:			US 2004-555767P	P	20040324
			WO 2005-US6277	W	20050301

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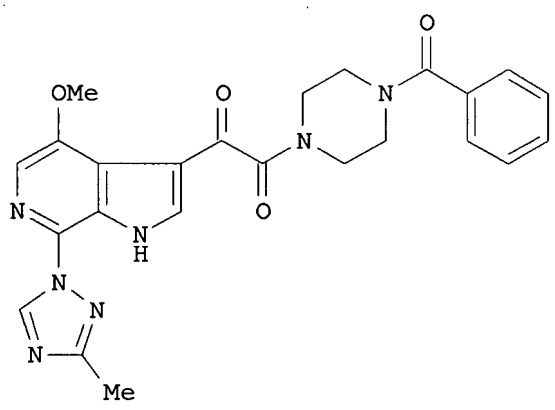


I

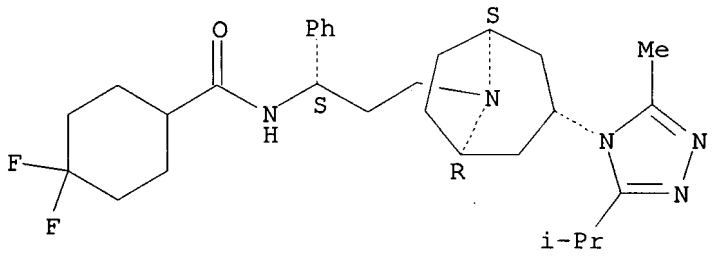
AB The invention encompasses pharmaceutical compns. and methods for using I in combination with other agents for treating patients with AIDS or HIV infection.

IT 376348-65-1, UK 427857
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(UK 427857; piperazine derivative combination with other anti-HIV agent for treating HIV infection)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 44 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1050855 CAPLUS
DOCUMENT NUMBER: 143:319113
TITLE: Methods using a combination of 1-benzoyl-4-[2-[4-fluoro-7-(1H-1,2,3-triazol-1-yl)-1H-pyrrolo[2,3-c]pyridin-3-yl]-1,2-dioxoethyl]piperazine and another anti-HIV agent for treating HIV infection
INVENTOR(S): Lin, Pin-Fang; Nowicka-Sans, Beata; Yamanaka, Gregory
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 14 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005215544	A1	20050929	US 2005-61273	20050218
WO 2005102328	A1	20051103	WO 2005-US5741	20050222

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-555768P P 20040324
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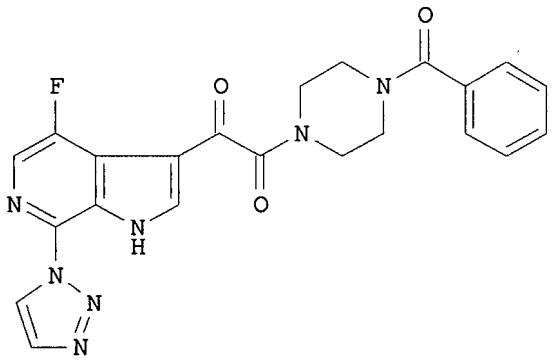


I

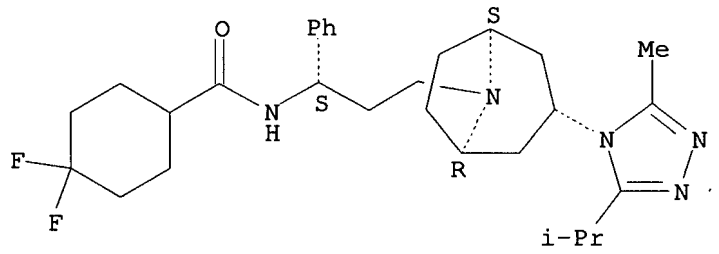
AB The invention encompasses pharmaceutical compns. and methods for using I in combination with other agents for treating patients with AIDS or HIV infection.

IT 376348-65-1, UK 427857
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(UK 427857; piperazine derivative combination with other anti-HIV agent for treating HIV infection)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 45 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:1050854 CAPLUS

DOCUMENT NUMBER: 143:319112

TITLE: Methods using a combination of 1-benzoyl-4-[2-(4,7-dimethoxy-1H-pyrrolo[2,3-c]pyridin-3-yl)-1,2-dioxoethyl]-piperazine and another anti-HIV agent for treating HIV infection

INVENTOR(S): Lin, Pin-Fang; Nowicka-Sans, Beata; Yamanaka, Gregory

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 14 pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 2005215543 A1 20050929 US 2005-57667 20050214
WO 2005102391 A1 20051103 WO 2005-US5417 20050218
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2004-555847P P 20040324
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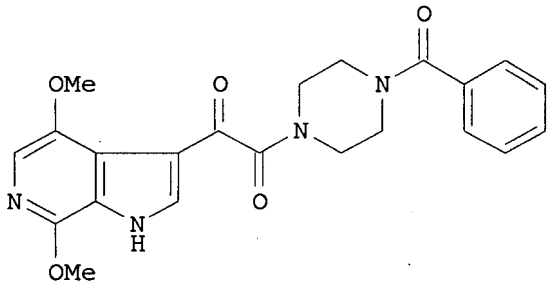


I

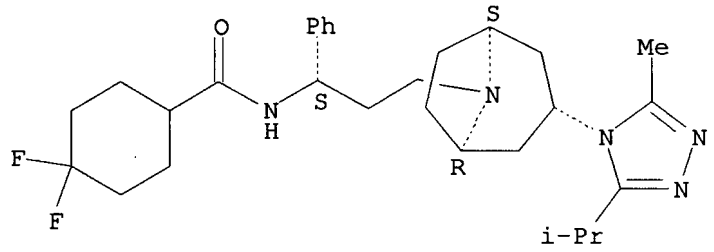
AB The invention encompasses pharmaceutical compns. and methods for treating AIDS and HIV infection employing I and at least one other agent used for treating AIDS or HIV infection.

IT 376348-65-1, UK 427857
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(UK 427857; piperazine derivative combination with other anti-HIV agent for treating HIV infection)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



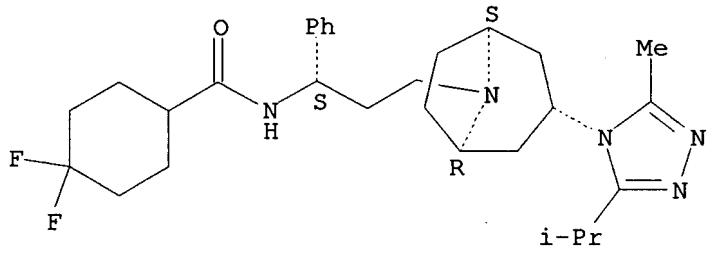
L6 ANSWER 46 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1022869 CAPLUS
DOCUMENT NUMBER: 144:63693
TITLE: Maraviroc

AUTHOR(S): Ginesta, J. Barretina; Castaner, J.; Bozzo, J.; Bayes, M.
CORPORATE SOURCE: Prous Science, Barcelona, 08080, Spain
SOURCE: Drugs of the Future (2005), 30(5), 469-477
CODEN: DRFUD4; ISSN: 0377-8282
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Despite the availability of several approved drugs for the treatment of human immunodeficiency virus (HIV) infection, the limited effectiveness of current antiretroviral regimens, mainly due to the emergence of resistance, makes the development of new agents necessary. Several novel compds. are being added to existing classes, but newer classes of antiretroviral drugs, such as HIV entry inhibitors, are also under development. Maraviroc is a novel small mol. that specifically antagonizes the chemokine CCR5 receptor required for efficient HIV entry. It displays potent and broad-spectrum anti-HIV activity and excellent pharmacokinetic and safety profiles. All these features and the promising results obtained in early clin. trials make this agent a good candidate for inclusion in combination therapies for HIV treatment. Maraviroc is the most clin. advanced CCR5 antagonist and has just entered phase III clin. trials.

IT 376348-65-1, Maraviroc
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chemokine CCR5 receptor antagonist maraviroc is HIV entry inhibitor and has potent and broad-spectrum anti-HIV activity and excellent pharmacokinetic and safety profile in patient with human immuno deficiency virus infection)
RN 376348-65-1 CAPLUS
CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 47 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:964176 CAPLUS
DOCUMENT NUMBER: 143:472249
TITLE: The discovery of the CCR5 receptor antagonist, UK-427,857, a new agent for the treatment of HIV infection and AIDS
AUTHOR(S): Wood, Anthony; Armour, Duncan
CORPORATE SOURCE: Department of Chemistry, Pfizer Global Research and Development, Sandwich Laboratories, Sandwich, Kent, CT13 9NJ, UK
SOURCE: Progress in Medicinal Chemistry (2005), 43, 239-271
CODEN: PMDCAY; ISSN: 0079-6468

PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

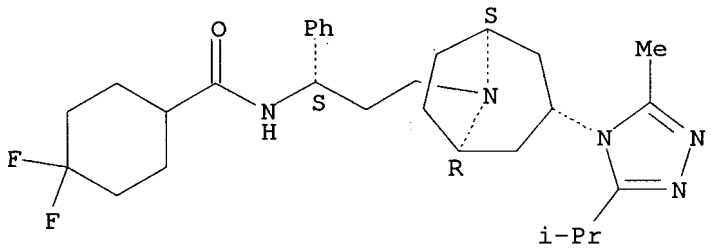
AB A review. The drug discovery program that led to the identification of UK-427,857, a prototype CCR5 antagonist with excellent potency against lab-adapted and primary HIV-1 isolates, as a clin. candidate for the treatment of HIV is described. In particular, strategies for minimizing cardiac toxicity while maintaining ADME properties commensurate with low dose are discussed.

IT 376348-65-1, UK 427857
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(UK 427857; CCR5 receptor antagonist UK-427,857 can possibly be used as therapeutic agents for treatment of human immunodeficiency virus and acquired immunodeficiency syndrome in patient)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 84 THERE ARE 84 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 48 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:698347 CAPLUS
DOCUMENT NUMBER: 143:194248
TITLE: Therapeutic combinations containing an amino acid amide HIV protease inhibitor
INVENTOR(S): Hammond, Jennifer Lou; Patick, Amy Karen
PATENT ASSIGNEE(S): Agouron Pharmaceuticals, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 25 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005171038	A1	20050804	US 2005-46260	20050128
AU 2005216710	A1	20050909	AU 2005-216710	20050117
CA 2555171	A1	20050909	CA 2005-2555171	20050117
WO 2005082362	A1	20050909	WO 2005-IB101	20050117

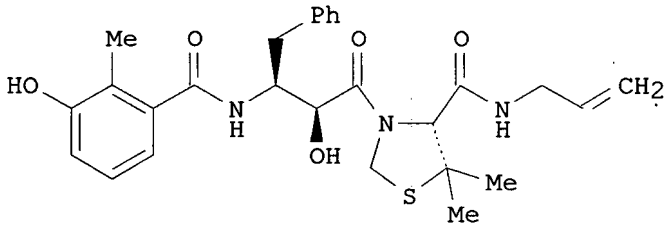
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,

AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1713470	A1	20061025	EP 2005-702264		20050117
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS					
BR 2005006493	A	20070213	BR 2005-6493		20050117
CN 1938017	A	20070328	CN 2005-80010030		20050117
JP 2007519704	T	20070719	JP 2006-550331		20050117
NO 2006003483	A	20060830	NO 2006-3483		20060731
MX 2006PA08632	A	20060904	MX 2006-PA8632		20060731
IN 2006DN04522	A	20070824	IN 2006-DN4522		20060804
PRIORITY APPLN. INFO.:			US 2004-540749P	P	20040130
			US 2004-615000P	P	20041001
			WO 2005-IB101	W	20050117

OTHER SOURCE(S): CASREACT 143:194248

GI



I

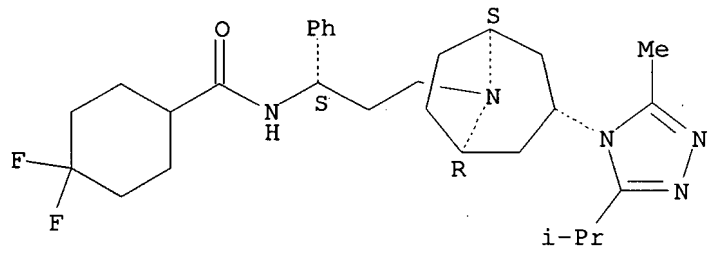
AB The invention is related to methods for treating an HIV infection by using a therapeutically effective amount of a combination of compds., including I and its related N-amide derivs. The invention is also related to compns. comprising certain compds. useful as inhibitors of the HIV protease enzyme and at least one addnl. therapeutic agent. In an XTT dye reduction method, I in combination with ritonavir acted synergistically against HIV-1 infection.

IT 376348-65-1, UK 427857
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy agent; compns. comprising an amino acid amide HIV protease inhibitor)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 49 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN

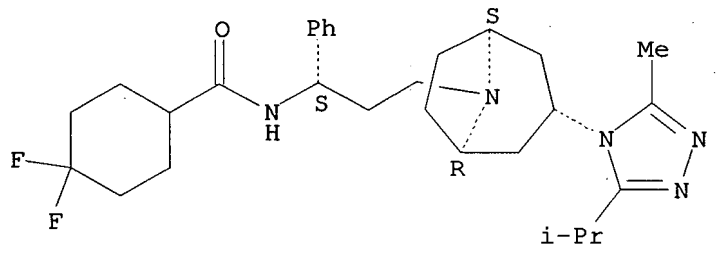
ACCESSION NUMBER: 2005:536932 CAPLUS
DOCUMENT NUMBER: 143:125633
TITLE: The appealing story of HIV entry inhibitors: from discovery of biological mechanisms to drug development
AUTHOR(S): Castagna, Antonella; Biswas, Priscilla; Beretta, Alberto; Lazzarin, Adriano
CORPORATE SOURCE: Clinic of Infectious Diseases, San Raffaele Scientific Institute, Milan, Italy
SOURCE: Drugs (2005), 65(7), 879-904
CODEN: DRUGAY; ISSN: 0012-6667
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Current therapeutic intervention in HIV infection relies upon 20 different drugs. Despite the impressive efficacy shown by these drugs, we are confronted with an unexpected frequency of adverse effects, such as mitochondrial toxicity and lipodystrophy, and resistance, not only to individual drugs but to entire drug classes. Thus, there is now a great need for new antiretroviral drugs with reduced toxicity, increased activity against drug-resistant viruses and a greater capacity to reach tissue sanctuaries of the virus. Two different HIV mols. have been selected as targets of drug inhibition so far: reverse transcriptase and protease. Drugs that target the interactions between the HIV envelope and the cellular receptor complex are a 'new entry' into the scenario of HIV therapy and have recently raised great interest because of their activity against multidrug-resistant viruses. There are several compds. that are at different developmental stages in the pipeline to counter HIV entry, among them: (i) the attachment inhibitor dextrin-2-sulfate; (ii) the inhibitors of the glycoprotein (gp) 120/CD4 interaction PRO 542, TNX 355 and BMS 488043; (iii) the co-receptor inhibitors subdivided in those targeting CCR5 (SCH 417690 [SCH D], UK 427857 GW 873140, PRO 140, TAK 220, AMD 887) and those targeting CXCR4 (AMD 070, KRH 2731); and (iv) the fusion inhibitors; enfuvirtide (T-20) and tifuvirtide (T-1249). The story, of the first of these drugs, enfuvirtide, which has successfully completed phase III clin. trials, has been approved by the US FDA and by the European Medicines Agency, and is now com. available worldwide, is an example of how the knowledge of basic mol. mechanisms can rapidly translate into the development of clin. effective mols.

IT 376348-65-1, UK 427857
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(UK 427857; addition of co-receptor CCR5 inhibitor UK 427857 to therapeutic armamentarium against HIV-1 offers new hope for treating HIV infected patient)

RN 376348-65-1 CAPLUS
CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 198 THERE ARE 198 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

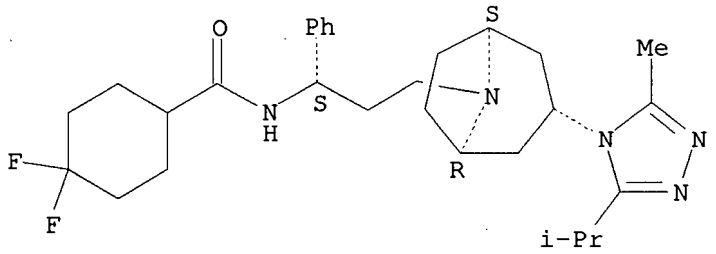
L6 ANSWER 50 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:314011 CAPLUS
DOCUMENT NUMBER: 143:90298
TITLE: Species differences in the disposition of the CCR5 antagonist, UK-427,857, a new potential treatment for HIV
AUTHOR(S): Walker, Don K.; Abel, Samantha; Comby, Pierre; Muirhead, Gary J.; Nedderman, Angus N. R.; Smith, Dennis A.
CORPORATE SOURCE: Department of Pharmacokinetics, Dynamics and Metabolism, Pfizer Global Research and Development, Kent, UK
SOURCE: Drug Metabolism and Disposition (2005), 33(4), 587-595
CODEN: DMDSAI; ISSN: 0090-9556
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB UK-427,857 (4, 4-difluoro-N-{(1S)-3-[exo-3-(3-isopropyl-5-methyl-4H-1,2,4-triazol-4-yl)-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl}cyclohexanecarboxamide) is a novel CCR5 antagonist undergoing investigation for use in the treatment of human immunodeficiency virus (HIV) infection. Pharmacokinetic and metabolism studies were performed in mouse, rat, dog, and human after single and multiple administration by oral and i.v. routes. The compound has physicochem. properties that are borderline for good pharmacokinetics, being moderately lipophilic (log D7.4 2.1) and basic (pKa 7.3), possessing a number of H-bonding functionalities, and with a mol. weight of 514. The compound was incompletely absorbed in rat (.apprx.20-30%) but well absorbed in dog (>70%). Based on in vitro studies in Caco-2 cells, UK-427,857 has relatively poor membrane permeability, and transcellular flux is enhanced in the presence of inhibitors of P-glycoprotein. Further evidence for the involvement of P-glycoprotein in restricting the oral absorption of UK-427,857 was obtained in P-glycoprotein null mice (mdr1a/mdr1b knockout). In these animals, AUC after oral administration was 3-fold higher than in control animals. In oral dose escalation studies in humans, the compound demonstrated nonlinear pharmacokinetics, with increased dose-normalized exposure with increased dose size, consistent with saturation of P-glycoprotein. The oral dose-exposure relationship of UK-427,857 in humans was not reflected in either rat or dog. In animal species and humans, UK-427,857 undergoes some metabolism, with parent compound the major component present in the systemic circulation and excreta. Elimination of radioactive dose was primarily via the feces. In rat, parent compound was secreted via bile and directly into the gastrointestinal tract. Metabolites were products of oxidative metabolism and showed a high degree of structural consistency across species.

IT 376348-65-1D, products of mono-oxidation in difluorocyclohexyl ring
RL: PKT (Pharmacokinetics); BIOL (Biological study)
(species differences in disposition of CCR5 antagonist UK-427,857 for treatment for HIV)

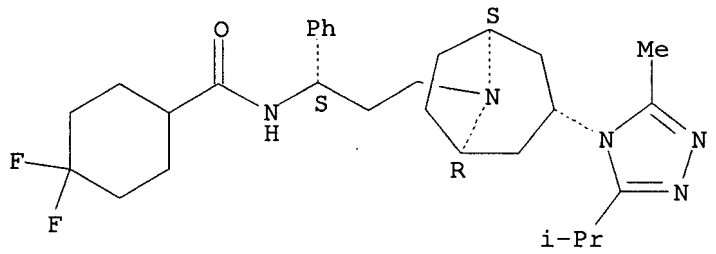
RN 376348-65-1 CAPLUS
CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



IT 376348-65-1
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(species differences in disposition of CCR5 antagonist UK-427,857 for treatment for HIV)
RN 376348-65-1 CAPLUS
CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 51 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:311526 CAPLUS
DOCUMENT NUMBER: 142:456334
TITLE: The CCR5 receptor-based mechanism of action of 873140, a potent allosteric noncompetitive HIV entry inhibitor
AUTHOR(S): Watson, Christian; Jenkinson, Stephen; Kazmierski, Wieslaw; Kenakin, Terry
CORPORATE SOURCE: Assay Development and Compound Profiling, GlaxoSmithKline Research and Development, Research Triangle Park, NC, USA
SOURCE: Molecular Pharmacology (2005), 67(4), 1268-1282
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 4-{[4-({(3R)-1-Butyl-3-[(R)-cyclohexyl(hydroxy)methyl]-2,5-dioxo-1,4,9-triazaspiro[5.5]undec-9-yl}methyl)phenyl]oxy}benzoic acid hydrochloride (873140) is a potent noncompetitive allosteric antagonist of the CCR5 receptor (pKB = 8.6±0.07; 95% Cl, 8.5 to 8.8) with concomitantly potent antiviral effects for HIV-1. In this article, the receptor-based mechanism of action of 873140 is compared with four other noncompetitive allosteric antagonists of CCR5. Although (Z)-(4-bromophenyl){1'-[(2,4-dimethyl-1-oxido-3-

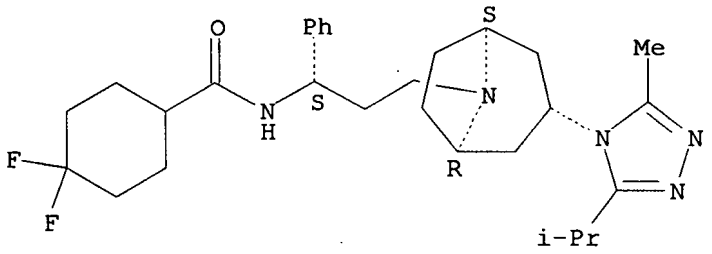
pyridinyl)carbonyl]-4'-methyl-1,4'-bipiperidin-4-yl}methanone O-ethyloxime (Sch-C; SCH 351125), 4,6-dimethyl-5-{[4-methyl-4-((3S)-3-methyl-4-{(1R)-2-(methyloxy)-1-[4-(trifluoromethyl)phenyl]ethyl}-1-piperazinyl)-1-piperidinyl]carbonyl}pyrimidine (Sch-D; SCH 417,690), 4,4-difluoro-N-((1S)-3-{(3-endo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl}-1-phenyl-propyl)cyclohexanecarboxamide (UK-427,857), and N,N-dimethyl-N-[4-[[[2-(4-methylphenyl)-6,7-dihydro-5H-benzocyclo-hepten-8-yl]carbonyl]amino]benzyl]tetrahydro-2H-pyran-4-aminium chloride (TAK779) blocked the binding of both chemokines 125I-MIP-1α (also known as 125I-CCL3, 125I-LD78) and 125I-RANTES (125I-CCL5), 873140 was an ineffectual antagonist of 125I-RANTES (regulated on activation normal T cell expressed and secreted) binding (but did block binding of 125I-MIP-1α). Furthermore, 873140 blocked the calcium response effects of CCR5 activation by CCL5 (RANTES) (as did the other antagonists), indicating a unique divergence of blockade of function and binding with this antagonist. The antagonism of CCR5 by 873140 is saturable and probe-dependent, consistent with an allosteric mechanism of action. The blockade of CCR5 by 873140 was extremely persistent with a rate constant for reversal of <0.004 h-1 (t1/2 > 136 h). Coadministration studies of 873140 with the four other allosteric antagonists yielded data that are consistent with the notion that all five of these antagonists bind to a common allosteric site on the CCR5 receptor. Although these ligands may have a common binding site, they do not exert the same allosteric effect on the receptor, as indicated by their differential effects on the binding of 125I-RANTES. This idea is discussed in terms of using these drugs sequentially to overcome HIV viral resistance in the clinic.

IT 376348-65-1, UK 427857
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CCR5 receptor-based mechanism of action of compound 873140, a potent allosteric noncompetitive HIV entry inhibitor)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 52 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:14522 CAPLUS
DOCUMENT NUMBER: 142:86614
TITLE: Compositions for down-regulation of CCR5 expression and reducing HIV entry into T-cells
INVENTOR(S): Redfield, Robert R.; Amoroso, Anthony; Davis, Charles E.; Heredia, Alonsa
PATENT ASSIGNEE(S): University of Maryland Biotechnology Institute, USA
SOURCE: PCT Int. Appl., 58 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005001027	A2	20050106	WO 2004-US15681	20040517
WO 2005001027	A3	20060126		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004251228	A1	20050106	AU 2004-251228	20040517
CA 2526122	A1	20050106	CA 2004-2526122	20040517
EP 1627048	A2	20060222	EP 2004-752660	20040517
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
CN 1805740	A	20060719	CN 2004-80016720	20040517
BR 2004010360	A	20060801	BR 2004-10360	20040517
MX 2005PA12352	A	20060711	MX 2005-PA12352	20051116
US 2006154857	A1	20060713	US 2005-281195	20051116
PRIORITY APPLN. INFO.:			US 2003-471453P P	20030516
			WO 2004-US15681 W	20040517

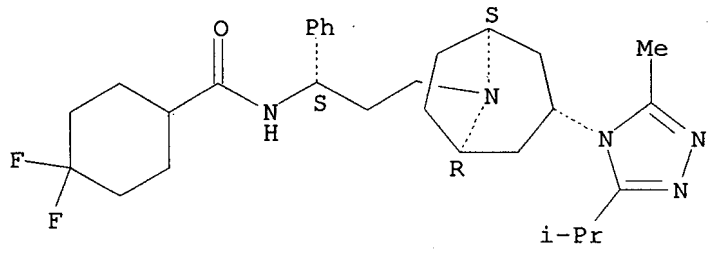
AB The present invention relates to the downregulation of surface receptor CCR5 expression through manipulation of the cell cycle in activated lymphocytes by administering a composition that arrests the G1 phase of the cell cycle, thereby reducing receptor sites for entry of HIV into T cells, and thus, the effects of HIV.
Further, a composition is disclosed that includes a G1 phase arresting agent and an antiviral agent, wherein the combination synergically enhances the activity of the antiviral agent.

IT 376348-65-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. for down-regulation of CCR5 expression and reducing HIV entry into T-cells)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 53 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:333850 CAPLUS
DOCUMENT NUMBER: 140:355836
TITLE: High-mannose oligosaccharide cluster conjugated with immunogenic protein for use as HIV vaccines
INVENTOR(S): Wang, Lai-xi
PATENT ASSIGNEE(S): University of Maryland Biotechnology Institute, Off. of Research Admin./ Tech. Dev., USA
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004033663	A2	20040422	WO 2003-US32496		20031014
WO 2004033663	A3	20060316			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2504755	A1	20040422	CA 2003-2504755		20031014
AU 2003282821	A1	20040504	AU 2003-282821		20031014
EP 1572963	A2	20050914	EP 2003-774819		20031014
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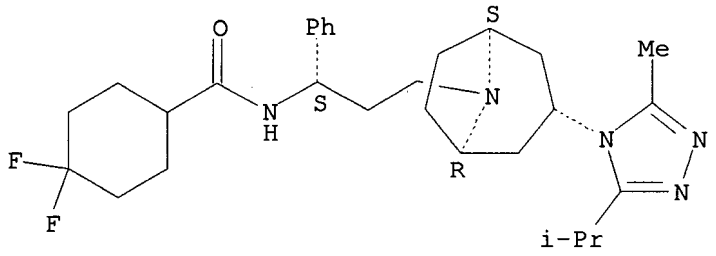
US 2005244424	A1	20051103	US 2005-531124		20050630
PRIORITY APPLN. INFO.:			US 2002-417764P	P	20021011
			WO 2003-US32496	W	20031014

AB The present invention relates to a constructed oligosaccharide cluster, optionally bonded to an immunogenic protein, that can be administered to a subject to induce an immune response for increasing production of 2G12 and/or used in assays as reactive sites for determining compds. that inactivate and/or bind the high-mannose oligosaccharide cluster. The high-mannose oligosaccharide cluster comprises ≥2 high-mannose oligosaccharides attached a scaffolding framework of monosaccharide, cyclic peptide, cyclic organic compound or 11-bis-maleimidetetraethyleneglycol. The high-mannose oligosaccharide that mimics high-mannose N-glycan of HIV-1 gp120 comprises Man9, Man8, Man7, Man6, Man5 or a combination thereof. The high-mannose oligosaccharide of the invention is derived from soybean agglutinin or chemical synthesized. The immunogenic protein is keyhole limpet hemocyanin, tetanus toxoid, diphtheria toxoid, bovine serum albumin, ovalbumin, thyroglobulin, myoglobin, cholera toxin β-subunit, Ig. and/or tuberculosis purified protein derivative Compns. comprising these clusters, methods of using these clusters and compns. are disclosed.

IT 376348-65-1, UK 427857
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(high-mannose oligosaccharide cluster conjugated with immunogenic protein for use as HIV vaccines)

RN 376348-65-1 CAPLUS
CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 54 OF 54 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:252478 CAPLUS
DOCUMENT NUMBER: 140:264479
TITLE: G1-phase arresting compounds for inducing increased levels of β-chemokines
INVENTOR(S): Redfield, Robert R.; Amoroso, Anthony; Davis, Charles E.; Heredia, Alonsa
PATENT ASSIGNEE(S): University of Maryland Biotechnology, USA
SOURCE: PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004024683	A2	20040325	WO 2003-US28697	20030912
WO 2004024683	A3	20040701		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2498934	A1	20040325	CA 2003-2498934	20030912
AU 2003266152	A1	20040430	AU 2003-266152	20030912
EP 1545539	A2	20050629	EP 2003-795698	20030912
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2006099170	A1	20060511	US 2005-527904	20050707
PRIORITY APPLN. INFO.:			US 2002-410714P P	20020913
			WO 2003-US28697 W	20030912

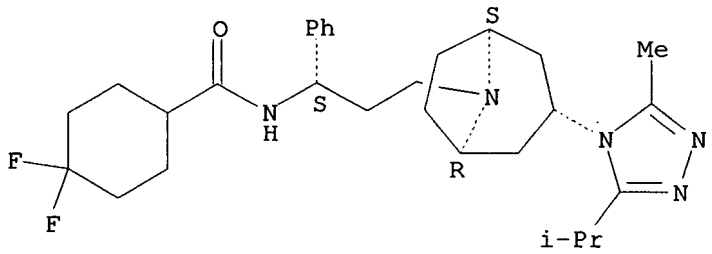
AB The present invention relates to methods for inducing increased levels and availability of β-chemokines by administering to a subject at least 1 G1-phase arresting compound, wherein the increased levels and availability of β-chemokines block chemokine/viral receptors thereby preventing or treating viral infections. The secretion of the β-chemokines by peripheral blood mononuclear cells in response to the activation started before lymphocytes entered the DNA synthesis phase of the cell cycle (S phase), reaches a peak by day 3 or 7 and then declined to low levels. The antivial activity is due the presence of the β-chemokines RANTES, and MIP proteins.
IT 376348-65-1

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(G1-phase arresting compds. for inducing increased levels of β-chemokines)

RN 376348-65-1 CAPLUS

CN Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-[(3-exo)-3-[3-methyl-5-(1-methylethyl)-4H-1,2,4-triazol-4-yl]-8-azabicyclo[3.2.1]oct-8-yl]-1-phenylpropyl]- (CA INDEX NAME)

Absolute stereochemistry.



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(FILE 'HOME' ENTERED AT 08:38:21 ON 19 OCT 2007)

FILE 'REGISTRY' ENTERED AT 08:38:30 ON 19 OCT 2007
L1 STRUCTURE UPLOADED
L2 0 S L1
L3 4 S L1 FULL

FILE 'CAPLUS' ENTERED AT 08:39:18 ON 19 OCT 2007
L4 78 S L3 FULL
L5 60 S L4 AND CCR5
L6 54 S L5 AND HIV

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	290.95	463.26
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-42.12	-42.12

STN INTERNATIONAL LOGOFF AT 08:42:25 ON 19 OCT 2007